GRAVES' DISEASE

WITH AND WITHOUT

EXOPHTHALMIC GOITRE

BY

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NEW YORK

WILLIAM WOOD & COMPANY

MDCCCCIV

PRESS OF STETTINER BROS.
52-58 DUANE STREET,
NEW YORK.

PREFACE.

The object of this treatise is to emphasize the fact that the constitutional and general derangements which are characteristic of Graves' Disease, constitute the disease, and not the condition of the thyroid gland, or of its accessories. To what extent a specific disorder of the thyroid is essential to the origin and continued progress of Graves' Disease, is rendered doubtful by the occurrence of cases of Graves' Disease in its severest and even fatal forms who show, however, no evidence of the thyroid being involved at all. In this treatise the clinical histories of twenty-eight patients who at no time showed any signs of Exophthalmic Goitre are compared, symptom by symptom, with the clinical histories of forty-two patients who did have Graves' goitre, each of both classes occurring in my own private practice. The comparison is made to demonstrate that this disease may have no recognizable, and therefore probably no necessary, relation to any state of the thyroid gland. The details of these histories may make tedious reading, but in no other way can this important clinical fact be established, involving as it then does very different conclusions about the pathology and treatment of Graves' Disease from the views of those who define "Basedow's Disease as an infection of the body through morbid activity of the thyroid gland."

NEW YORK, 23 FORTY-SEVENTH STREET, EAST.

March, 1904.

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In no disease are the external features more obvious or striking than in a typical case of Exophthalmic Goitre. Aside from the prominent tumor and deformity of the neck, the peculiar appearance of the eyes alone would suffice to attract attention. It was but natural, therefore, that the malady should acquire a name from these two obtrusive symptoms. But another result of the prominence of these symptoms was the suggestion that they bore a causative relationship to the disease itself. This has led many writers, therefore, to regard Graves' Disease as primarily due a specific derangement of the thyroid gland, and to base their deductions as to its pathology and treatment chiefly on this assumption.

The most cursory inspection of the very extensive literature connected with this interesting malady will suffice to illustrate the exclusive sway of this conception; and full weight, therefore, should be accorded to the considerations which have been adduced to support it. Thus it has been pointed out by Möbius and by other writers that the symptoms of myxedema, which are due to deficiency of thyroid secretion from atrophy of the gland, are just the opposite to those of Exophthalmic Goitre, in which the thyroid seems to hypertrophy from over-action. Hence, it is inferred that Exophthalmic Goitre is caused by the presence in the blood of an excessive quantity of thyroid secretion; and this surmise is further supported by the alleged production of some of the circulatory symptoms of Graves' Disease, by the administration of large doses of thyroid extract.

But there are certain important clinical facts to be taken into

account, before such a conclusion can be regarded as settled. In the first place extensive morbid changes often do occur in the thyroid, so as to cause very pronounced goitres, and yet with no accompanying symptoms whatever which are characteristic of Graves' Disease. For the fact should be emphasized that the clinical course of Graves' Disease is marked, quite apart from the goitre and exophthalmos, by a train of numerous special symptoms, most varied in character and of the widest distribution, and which are entirely unlike those accompanying any other form of goitre, whether parenchymatous, adenoid, cystic or malignant. Clinically, no contrast is more complete than that between the accompaniments of two equally developed goitres, one of the ordinary parenchymatous, or cystic, variety, and the other in a typical case of Graves' Disease. The former is a goitre, and not much else—a local tumor causing little besides local symptoms; with the latter scarcely a function of life remains unaffected, as shown by a corresponding remarkable variety of manifestations.

Moreover, it is the presence of these peculiar and specific symptoms which alone proves the existence of Graves' Disease, and which of themselves would serve to differentiate it from any other known malady, because in no other affection are such symptoms grouped together in similar fashion. But it has long been noted that the severity of the illness in a case of Exophthalmic Goitre always depends upon the degree of development of these general or constitutional symptoms, and not at all upon the degree of enlargement of the thyroid itself, for this varies greatly in different patients, or in the same patients at different times, without any definite relation to other conditions.

Much the most serious difficulty, however, is encountered by the occurrence of undoubted cases of Graves' Disease, in patients who show no apparent signs of affection of the thyroid gland whatever, and likewise no exophthalmos. These cases cannot be mistaken because, as above remarked, there is no other affection in which a similar concurrence of such pronounced and peculiar symptoms happens. Most authors, who speak with any wide experience with this disease, refer to such cases, but with varying and uncertain comments about them.

Thus Möbius[1], who defines "Basedow's Disease as an infection of the body through morbid activity of the thyroid gland," says: "Beside the picture, rich in symptoms, stand the aberrant forms, in which often only some few symptoms are demonstrable, and probably the extent of those aberrant forms is much greater than is generally supposed." . . .

"Diagnostic difficulty occurs only in incomplete cases, or in those with other slight non-characteristic symptoms, when a definite diagnosis is not always possible. Gordon Hill has collected a number of observations which show that a definite line between Basedow's Disease and so-called tachycardia does not exist. These histories show, without doubt, that in the majority of cases actual Basedow's Disease was present."

Marie[2] says, as to the forms of the malady, one can enumerate only complete, incomplete and abortive (frustre) forms. In the abortive forms are included those varieties in which there are neither exophthalmos nor goitre. The diagnosis, however, can be made by seeking the symptoms of secondary bearing, such as trembling, diarrhœa, bulimia, etc.

Oliver[3] remarks: "Basedow's Disease is quite distinct from ordinary goitre, and yet in both cases the thyroid gland is enlarged. In Exophthalmic Goitre, however, it is not alone a question of the enlargement of the thyroid gland. There is behind it an amount of cardio-vascular and nerve disturbance which is of far greater importance than the enlargement of the thyroid. . . . Long before exophthalmos, or fullness in the neck, has been observed there may have been palpitation. This may go on for a considerable time, and the exophthalmos be only gradually developed, or not at all."

A. Maude[4] says: "There is a gradual growth of opinion that the symptom complex is due to the production (or non-elimination) in the thyroid itself of some toxin, which acts on the whole nervous system. . . . This toxin may be first formed in

[1] Möbius, in Nothnagel, Special Pathology and Therapy, Vol. xxii., p. 8.

[2] Annales de Med. Scient. et Pratique, 1893, p. 249.

[3] International Clinics, 1893, p. 98.

[4] Brain, 1894. Brit. Med. Jour., Oct. 21, 1893; June, 1896.

the alimentary canal, and then remain in the circulation on account of excessive disturbance of the thyroid."

I may add that I was myself inclined to regard such cases as merely undeveloped instances of this complaint, or aberrant forms analogous to those variations from the ordinary type which are met with in every chronic disease, until a wider experience convinced me that such was far from being the truth. Instead of being exceptional, or simply occasional examples of Graves' Disease, my records show that they are of frequent occurrence; and what is more, the malady in them, instead of being abortive or incomplete, has furnished in my experience as many of the worst and most fatal forms of the disease as among the patients with goitre. A really severe case of Graves' Disease, whatever its form, is a formidable malady, and quite sui generis and uniform in the terminal symptoms which precede death. Hence, when I had repeatedly met with instances of the kind of extreme gravity, and yet who never showed any signs pointing to the thyroid gland any more than to the spleen, or to other ductless gland, I was led to look for examples of the same affection without goitre, but milder in their course. I am now convinced that Graves' Disease, without goitre, is more common than is usually supposed, without its being at all incomplete because of the absence of thyroid enlargement, for the special constitutional derangements of the malady, both in kind and in degree, are quite the same in both classes. I am also assured that others will have the same experience with myself, when once they are freed from the impression that to be a case of Graves' Disease the patient must show an enlarged thyroid.

It is the purpose, therefore, of this treatise to demonstrate by the clinical histories of 28 patients, who at no time showed either exophthalmos or goitre, with the clinical histories of 42 patients with fully developed exophthalmic goitre, that the former were as much cases of Graves' Disease as the latter. I may here state that all these patients of both classes have been under my own observation in my private practice, or in consultation with other physicians; my notes beginning with the year 1888. I might add a number of others from my hospital experience, but for the fact that hospital patients with this chronic

complaint rarely remain long enough under observation to make their histories sufficiently complete. The list also of patients without goitre might be much extended by including a number of incipient or less developed cases, but as the diagnosis might be called in question, they have been omitted.

As it stands, this comparison between these two classes, those without and those with exophthalmic goitre, will suffice, it seems to me, to prove not only that both classes had the same disease, but that those who had no goitre suffered as much from it as those who had goitre. In two of my own cases without goitre the disease was not only prolonged, but was plainly the sole cause of death, so that in them at least it could hardly be termed either frustre or latent. Before I saw them the proper term rather should have been "unrecognized," and is another illustration of the disadvantage of naming a disease after symptoms, because the entire absence of symptoms in the eyes and in the thyroid prevented the true disease from being diagnosed in them for many months ere they came under my observation. Every consultant of much experience has doubtless had cases of tabes brought to him which had been unrecognized, because they did not show "locomotor ataxia"; and repeatedly have I been called in consultation by physicians who were quite at a loss to determine what their patients were suffering from, simply because of the name exophthalmic goitre.

A conclusive demonstration that Graves' Disease may in a large proportion of cases be complete in all essentials, and run its course even to a fatal issue without any appreciable affection of the thyroid gland, must have an important bearing upon its pathology and upon the treatment of the malady.

Implication of the thyroid, then, instead of holding a primary relationship to the disease, becomes as secondary to its true cause, as the greatly enlarged spleen in some cases of chronic ague is secondary to malarial infection. But to substantiate this statement, it must be satisfactorily shown that Graves' Disease without goitre or exophthalmos can be definitely diagnosed as such. It is obvious, that in this particular there should be no room for uncertainty, for the entire discussion depends upon the diagnosis, in each case, being unquestionable. To show that

this can be so, I have arranged the characteristic symptoms of Graves' Disease under the following twenty-eight heads, irrespective of goitre and exophthalmos. A larger or more varied list of special and distinguishing signs certainly can hardly be paralleled in any other specific disease.

The distinctly characteristic symptoms of Graves' Disease, aside from goitre and exophthalmos, are as follows:

1. Tachycardia.
2. Palpitation.
3. Nervousness.
4. Muscular tremors, general and special.

Pareses: (*a*) general muscular weakness; (*b*) local weakness of the knees; (*c*) of the voice; (*d*) abasia; (*e*) aphasia.

6. Local paralyses.
7. Mental symptoms: (*a*) depression; (*b*) changes of disposition; (*c*) mania.
8. Special affections of the ears.
9. Special affections of the eyes.
10. Affections of smell.
11. Pains: (*a*) general; (*b*) localized in neck, finger tips, toes, heels, and in external ears; (*c*) muscular pains.
12. Headaches.
13. Vertigo.
14. Paræsthesiæ.
15. Characteristic disorders of the stomach.
16. Characteristic disorders of the intestines.
17. Bulimia.
18. Emaciation.
19. Insomnia.
20. Loss of hair.
21. Pigmentation of the skin.
22. Itching.
23. Sweating.
24. Vesical irritability.
25. All symptoms worse in the morning.

26. Disease chronic.
27. Family complaint.
28. Death sudden, from syncope.

A further clinical fact should be emphasized, namely: That the majority of these symptoms, whether motor, sensory or nutritive, are peculiar in the forms which they assume in Graves' Disease and unlike similar symptoms in other affections, as the following particular consideration of them will demonstrate. One only needs to study this most complete clinical picture in detail to become convinced, when in any given case he finds it exactly reproduced both in chief and in minor features, that he is confronted with none other than Graves' Disease, though both thyroid enlargement and eye protrusion be wholly wanting. It is not until one becomes familiar with the remarkable conjunction of such diverse symptoms, that he recognizes the singular definiteness of this disease. In each of my fatal cases, without goitre, scarcely one of the above outlined characteristics failed to occur: while with the remainder the average frequency of their incidence is the same between those with and those without goitre.

1. *Tachycardia.*—The first of these specific symptoms of Graves' Disease is the long-continued rapid action of the heart. To be characteristic, the pulse should range from 90 to 120, or more, and such frequency should be chronic and persistent, always present at every examination, through months, and it may be years, and be entirely independent of any other cause of tachycardia. Much care should be taken to be certain that such is the case, for when the absence of every other known cause of undue frequency of the heart beat is assured, the pronounced tachycardia of Graves' Disease will then be recognized as undoubtedly peculiar and specific; and, therefore, dependent upon its own particular cause without the participation of any different element or condition.

These postulates would exclude, to begin with, all cases of rapid action of the heart from nervous excitement. Patients with Graves' Disease very generally appear to be laboring under some undue nervous agitation which makes the hands shake and

the voice tremble; and it is easy, therefore, to mistake their tachycardia for the rapid pulse of merely excited patients, particularly as they themselves often complain that they are nervous; and this mistake is all the more likely, if the existence of Graves' Disease does not occur to the physician because of the absence of goitre and exophthalmos. But time and repeated examinations will show the difference from a merely excited pulse to be great and unmistakable. Those who are only nervous will ere long calm down and the pulse rate will fall accordingly. The Graves' pulse never calms down, however quiet the patient may become. It runs as fast or faster than in any fever or inflammation, by day and by night, and also in sleep, with less change at each counting over long periods than in any other complaint.

Equally easy is it to exclude the quick pulse so often present in anæmic or debilitated patients. Physical exertion is the commonest excitant of the pulse in such conditions and it soon falls after rest, particularly after lying down. But the tachycardia of Graves' Disease may continue with little or no change, though the patient be kept recumbent for months at a time.

The tachycardia of all fevers can be at once and conclusively excluded by the thermometer, which in Graves' Disease (at least when the disease has become chronic) rarely varies from normal, though occasionally the temperature is subnormal. Graves' Disease cannot be termed a febrile complaint, and hence its pulse rate has no connection with such a condition.

Inflammatory or organic changes in the heart itself can equally be excluded as causes of this tachycardia, for careful examination will demonstrate that this organ is only functionally deranged. Occasionally systolic murmurs are detected, but they are very variable and bear no constant relation to the other symptoms, while in much the majority of cases no murmurs are heard. Instead, it is remarkable how long this overaction of the heart may continue in Graves' Disease without showing post mortem either hypertrophy, dilatation or inflammatory lesions of any kind. In others, the heart walls are found post mortem more or less degenerated, but not more so than the texture of other organs which suffer alike from the widespread disorders of nutrition and wasting which precedes death in this complaint.

Tachycardia is an occasional accompaniment of certain cerebro-spinal affections, particularly tabes; but these in turn can be excluded by the entire absence of their characteristic symptoms in Graves' Disease. In some cases also of chronic disease of the kidneys the pulse may be habitually frequent, but though albuminuria may be found in patients with Graves' Disease, yet its presence is both variable and temporary in those who show it, while in the great majority it is uniformly absent. The presence of albuminuria in Graves' Disease was formerly much commented upon, particularly by Begbie. This was at a time when albuminuria was considered as equivalent to Bright's Disease. But after careful examination, I can say that its occurrence in Graves' Disease is neither constant nor significant.

After all such causes of rapid heart action are excluded, the pronounced and strikingly persistent tachycardia of Graves' Disease then appears as a singular, and virtually as a pathognomonic symptom. No other form of tachycardia compares with it for long continuance. I have known it to remain unchanged for nine years; and in more than half of the cases it lasts over two years. This symptom, therefore, of itself would suggest its dependence on a toxæmia of a functional kind, for none of the other causes of tachycardia enumerated would continue to so affect the heart without the gravest disorders of nutrition developing elsewhere long before the term in which it continues with Graves' Disease.

It must hold also some important relation to the disease itself which is far more constant than that of either the goitre or the exophthalmos, for I found it absent in only two of my 70 cases.

The first of these is a patient with goitre, but without exophthalmos, and which I would not exclude because of the presence of other characteristic signs. This patient's mother also had goitre, but without exophthalmos. The second is a case without goitre or eye change, but with tremor and other marked symptoms, and she has a sister with pronounced exophthalmic goitre. Both these cases are of recent origin comparatively, and the tachycardia may not yet have had time to develop. Therefore, this symptom alone when definitely recognized in a patient may prove an invaluable clue to the explanation of many cases which

otherwise would be very puzzling on account of the great variety of the symptoms, of which my list affords many illustrations. It not infrequently happens that the patients themselves are not aware of their tachycardia when they apply for advice for the other derangements of the complaint. At other times they mention having first noticed the heart being affected long after they had suffered from the other symptoms; but it is then probable that tachycardia would have been detected had the pulse been counted by a physician.

These considerationes definitely indicate that this peculiar state of the heart, characterized by such continuous over-action, constitutes one of the essential symptoms of Graves' Disease. But in my experience, as hereinafter detailed, it is found fully as often and quite as marked in all its features in patients who show no evidence of thyroid enlargement as in those who do. While the other symptoms and accompaniments of the complaint in no way differ between the two classes.

2. *Palpitation.*—Palpitation as a symptom is quite distinct from tachycardia, for the latter may exist to a high degree, as in fever, and yet the patient be hardly cognizant of it. The patient, on the contrary, is always conscious of palpitation, and frequently is much alarmed by it. He feels the heart stop, then bound violently, then beat irregularly and then rapidly, all in turns; and if it occurs at night, it banishes sleep by the nervousness which it occasions. Nocturnal palpitation is of frequent occurrence in Graves' Disease, and not uncommonly wakens the patient suddenly after midnight. It has no relation to the degree of tachycardia, for I have known it greatly to distress patients whose tachycardia was but moderate. In one case with goitre, and in one without goitre, it caused as pronounced a sense of impending death as in angina pectoris. Paroxysmal tachycardia is an independent affection from Graves' Disease, and in my experience occurs oftener in elderly men than in women. One patient, however, without goitre (æt. 40), had paroxysms of extreme rapid action of the heart, usually lasting two days and then returning to normal; and this intermittency of the tachycardia remained a feature of her case, while the other symptoms

of Graves' Disease continued for months, until she gradually recovered her health.

In advanced cases of the disease, equally among both classes, the pulse may be found intermittent as well as rapid. This is not a favorable symptom, and indicates cardiac exhaustion. Still more ominous is a decided fall in the pulse to normal or below normal in frequency, without improvement in other respects, as it may be a sign of impending collapse. In one patient, however, with goitre, seen in consultation, the pulse was extremely irregular, as well as intermittent and very rapid. But though her physician stated she had had this pulse for seven years, she otherwise enjoyed good health. I have my doubts whether the tachycardia in her case was not wholly due to pressure by the tumor in the neck. In its other qualities, the pulse of Graves' Disease varies with different patients, in quite a number showing comparatively high tension, not unlike the pulse of chlorotics. At one time I supposed that the pulse must always be of low tension, owing to the general relaxation of the arteries, until I met with instances of the opposite condition of high tension, without any renal complication to account for it.

Nervous Symptoms.—Functional derangements of the nervous system occur in Graves' Disease, with a greater variety in the individual symptoms than in any other complaint, not excepting hysteria. But though so varied, yet they will be found to be definitely characteristic of the disease in the mode and sequence of their occurrence, and in their relation to the other derangements. It is this association with the other symptoms which identifies them as belonging to this complaint, and not to different nervous disorders with which they might otherwise be confounded.

3. *Nervousness.*—The first to be mentioned, as often it is the first which the patients themselves recognize, is a persistent and causeless nervousness. It has much the character of mental agitation, not unlike that accompanying a sense of fright. This has led some writers to look for fright as the true cause of the disease itself. Hector Mackenzie goes so far as to suggest that if some patients cannot remember any occasion of sudden alarm, yet an ancestor of theirs may have experienced a great scare and

then transmitted its effects to them by descent! My own experience as to fright has been very different. In not one of the whole series, either with or without goitre, is fright mentioned as an antecedent. A number of them, as will be seen in the records, admitted the antecedent existence of a nervous strain, such as worry or bereavement, but not one could remember any sudden alarm as the cause. The contrast in this respect to chorea is quite noteworthy. But in all such enquiries of patients some precautions are advisable. I have known physicians so imbued with the belief that some mental experience must be the beginning of the illness, as to insist on the patient's trying to remember something of the kind, until the patient begins to think so too. But such clinical records are worthless compared with the voluntary narrative of the patient, aided only by apparently casual questions on such points by the examiner. Left to themselves the majority of my cases stated that they could not understand why they were so nervous, and repeatedly they have expressed their mortification at the condition when they had every reason to be otherwise.

The degree, as well as the form, with which patients are affected with this nervousness varies. Some do not complain of, nor manifest, any nervousness; others say that they are only so occasionally, others, again, experience it so constantly that it constitutes one of the chief miseries of the complaint. Thus, in two patients (who were males) they described it as simply maddening when it came on as if in violent paroxysms. With some, it takes the form of pure depression of spirits, and in each of these it partakes of the curious feature to be mentioned soon as a marked characteristic of other symptoms as well of Graves' Disease, of being worse in the mornings. But what we would emphasize here is, that this nervousness is equally represented in all its aspects in the histories of those with goitre and those without goitre. In the 42 cases with goitre, it was not complained of as marked in 12 cases; moderate in 8, and extreme in 21. In those without goitre, it was not complained of in 9; moderate in 3; and was extreme in 18. In only two of the female patients without goitre could this nervousness be said to resemble hysteria at any time. These are just the class of patients, how-

ever, in which this diagnosis is often mistakenly made, solely on account of the nervousness. But besides the tachycardia, which is altogether too continuous and persistent to go with hysteria, the characteristic mental accompaniments of hysteria are conspicuous by their absence. They are but rarely emotional. They are not affected by sympathy any more than a case of typhoid fever, and they look the physician straight in the face and show no response to suggestions, but are prompt to deny symptoms which they do not have; and they remain consistent in their descriptions of the symptoms which they do have, with no variation in the story for months; while they are always ready to acknowledge an improvement in symptoms, when that occurs.

On the other hand, of four patients without goitre who were males and who suffered from nervousness, not one admitted venery, seminal emissions or spermatorrhea.

Motor Symptoms.—Akin to the subjective symptom of nervousness is the muscular tremor, which when general presents a striking similarity to the bodily tremor of fear or even terror.

4. *Muscular tremors.*—Of the 42 cases of goitre, it was present in 37, and not recorded in two, though it may have been present in them also. Of the 28 cases without goitre, it was present as a general tremor, but moderate, in 14; very pronounced in 5; and in 9 it was not marked. In one of these latter general painful muscular stiffness seemed to replace the tremor. The earliest development of tremor I have found to be in the eyelids when closed, though it may disappear when there is much protrusion of the eyeball. In the whole list of the goitre cases eyelid tremor was absent in only three, one a male, though he had tremor of the right hand which seriously affected his handwriting, and tremor of the legs. In three goitre cases, the only tremor observable was in the eyelids. Of the non-goitrous cases, the eyelids were affected in every one, and was the only part affected in one. This tremor of the lids, therefore, is of value in patients who show no goitre as a confirmatory sign when other symptoms are present, and it may indicate the first stage in that paresis, which later gives rise to both the Stellwag and von Græf symptoms.

The patients often describe their own consciousness of the

tremor as an inward trembling, as they would the subjective sensation of fear; but as a rule the tremor is limited both in extent and in site. Thus, in 26 cases of the goitrous cases the hands were chiefly affected; and in 19 of those without goitre. In six of the goitrous cases the right hand was so tremulous that they could not write with it, but with all of the six the tremor would pass off by evening, so that they then could write. In eight of the non-goitrous cases, the shaking of the right hand was extreme; three could not write; and two could not sew in the morning, but they could so use the right hand in the evening. In 11 the shaking of the right hand was moderate, in the remaining 9 no tremor was recorded. In one of the non-goitrous cases (a male) the hand tremor was the cause of his coming for advice, as it interfered with his signing checks as cashier of a firm. I found the trouble in his case in no sense an occupation neurosis, and afterwards his sister came with pronounced Graves' Disease. In one case (a clergyman) the shaking of the right hand preceded by three years the first sign of goitre. In one goitrous case (a married lady) there was eyelid tremor with ptosis of the right eyelid, pronounced tremor of the tongue and constant inward tremor; but the right hand was not involved at all. In one non-goitrous case, the left arm was almost alone affected and occasionally became paralyzed. Tremor in the lower extremities, aside from the knees, is not as common as in the arms. The tongue is often involved, and the tremor in it is generally fibrillar, while not un-often the muscles of the face and lips are involved.

The tremor of Graves' Disease is never as general or pronounced as the tremor of paralysis agitans, and it is in no sense a rhythmic tremor, but rather jerky and most pronounced on voluntary movement. I have never seen it resemble chorea, as stated by some writers, nor myotonia; and only in rare cases are there active contractions in the affected muscles, the tremor being more like that of muscles over-taxed by strain. The rate of the tremor is 8.5 per second; and, therefore, faster than senile tremor, which it otherwise resembles.

5. *Pareses.*—Another motor symptom found alike in both those with and those without goitre is weakness of the knees;

for though the patients may experience such a sense in the legs generally, yet it is usually referred to these joints particularly, and in most cases solely, and not to the ankles or hips. It is as often felt in walking on a level as in going up stairs, but most of all in descending stairs. After a time the knees may suddenly give way, and the patients fall so quickly that they scarcely have time to prepare for it, and yet they quickly rise again as if they had simply stumbled, instead of being paralyzed. Out of the 42 cases with goitre, weakness of the knees was especially noted in 24; and of the 28 cases without goitre, it was noted in 22, and not in 6. Actual abasia occurred in 7 of those with goitre, and in 4 of those without goitre.

Weakness of the voice, not amounting to aphonia, but annoying to the patient, occasionally occurs. It was complained of in 11 of the goitrous cases, one, a clergyman, being occasionally prevented by it from preaching. It was also specially mentioned by 4 of the patients without goitre. This symptom, therefore, has no relation to the presence of the tumor in the neck, and in the cases with goitre its degree bore no relation either to the position or to the size of the goitre . A sense of constriction in the throat, sometimes accompanied with pain, was complained of in three cases with goitre, and in three cases without goitre. The latter thought they must have a swelling of the throat on account of this feeling, when I could detect no enlargement of the thyroid.

Both aphasia (motor) and paraphasia are occasional symptoms. The most marked example of the kind was in a patient (over 60 years of age) without goitre, but who had attacks of severe vertigo, after which she would remain aphasic for some hours. Another example of the kind occurred in a lady with goitre and extreme exophthalmos, the loss of speech coming on suddenly and giving her much annoyance. A third case, in a non-goitrous patient, occurred as one of the early symptoms of the disease. Paraphasia was more common, but in no case resembled the speech disturbances of hysteria. Attacks of aphasia occurred in three cases with goitre and four cases without goitre.

6. *Local paralyses.*—Local paralyses are of occasional occurrence. In one case with goitre, there was ptosis of the right eye-

lid, and in another ptosis of the left eyelid. In one case with goitre, Bell's paralysis temporarily occurred on the right side of the face three years before she had goitre, and then recurred on the left side three years after she had goitre, and persisted for fourteen months. In one case without goitre, the same paralysis developed with attacks of spasmodic tic, affecting especially the left eyelid and the left muscles of the face.

7. *Mental symptoms.*—In a certain proportion of patients with Graves' Disease some symptoms referrible to the mind became observable. The commonest are changes of disposition, manifested in irritability of temper, or a peculiar wilfulness or obstinacy in refusing to act on advice. In one (a male), there was unnatural gayety of manner. In 14 of the goitrous, and in 12 of the non-goitrous cases, morning mental depression was particularly complained of. In advanced cases delirium may occur, and was present in the four fatal cases; two with goitre, and one without goitre, became maniacal before death. The fourth fatal case, also without goitre, became delirious, but not excited, before she died.

One severe chronic case recovered from both exophthalmos and goitre, so that she resumed her occupation as a school teacher; but from over-application to her duties she became insomnic, and then passed into melancholia, which necessitated her removal to an asylum, where she still remains after four years. With the full development of her insanity the symptoms of Graves' Disease, including the tachycardia, disappeared.

One case (a married lady) had always been eccentric in her conduct and opinions, but on the development of Graves' Disease became a confirmed paranoic. Such instances of mental disturbance, aside from the terminal developments above mentioned, did not occur in more than five per cent. of both classes in my records. With the majority no symptoms of the kind were ever noted, both mind and disposition remaining unaffected throughout. This fact is the more noteworthy, because many of them were much distressed with their nervousness, and yet at no time did they become emotional or hypochondriacal, thus showing that their nervousness, like the tachycardia, was specific and not secondary to mental states.

SENSORY DERANGEMENTS.—The sensory symptoms of Graves' Disease are extremely varied, some of them special and quite peculiar to the disease, so that they may serve to confirm the diagnosis; while others so resemble the symptoms of other diseases as frequently to lead to mistakes in diagnosis.

8. *Special affections of the ears.*—Of the special senses the ears are oftenest affected. Of the 42 cases with goitre, they were not affected in 24. In the remaining 18, a permanent diminution of hearing in both ears was present in one; marked deafness of the left ear disappearing with the cure of the disease in one; tinnitus in the left ear in four, one complaining of it as distracting for over a year, but it ceased altogether with improvement of the disease. A sense of throbbing in both ears occurred in three, limited to the left ear in one; in one case there was violent throbbing in the left ear, with tinnitus in the right. The most peculiar affection, however, was a pain described as a sense of tenderness to touch of the auricles, making it uncomfortable to lie upon them. This was referred to the left ear alone in one; to both ears in three; to the right ear in one, along with tinnitus in the left ear. In three the pain was referred not to the ears, but to the neck below the mastoid. The painful ears were often red, but sometimes not.

In 28 cases without goitre, the ears were not affected in 11. Among the remaining 17, there was marked loss of hearing in both ears in one, with complete restoration with improvement of the disease; deafness limited to the left ear in two; tinnitus in both ears in 7, most pronounced in left ear in one; tinnitus in left ear only in 5. Pain in both ears in 6, but much more marked in the left ear in two. Pain limited to the left ear in four; limited to the right ear in two; much tenderness to touch of the external ear in three; most pronounced on the left side in two, and on the right in one. Throbbing in the ears in three. In one the pain in the left ear was accompanied with severe attacks of vertigo.

In all cases, in both those with and those without goitre, except one with goitre, the relief of the ear symptoms was among the first signs of improvement in the disease itself. In two cases, without goitre, both on the left side, the pain extended from the

ear down the neck. As in the cases with goitre, the greater tendency to implication of the left ear was pronounced. In fact there could be no greater resemblance in the particulars of the ear derangements than that between the two classes; and taken as a whole, they constitute a special form, unlike any other aural derangement, for no signs of any inflammatory process in the ears were ever discovered on examination, except in one case with goitre who, however, had had otitis media for years before she became subject to Graves' Disease.

9. *Special affections of the eyes.*—It is singular that with the special affection of the eyes, which has given a name to Graves' Disease, ocular symptoms of a functional kind I have found to be both less frequent and less pronounced in this complaint than the symptoms referred to the ears. Thus, in the 42 cases with goitre, no complaint was made of the eyes in 32; 6 complained of frequent pains referred to the eyeballs; one was much troubled with persistent retinal images when the eyes were closed, but had no pain. Colored spectra occurred in two, limited in one to the right eye. In not one of my cases with exophthalmos was the sight impaired.

Among the 28 cases without goitre, the eyes were not complained of in 13. There was pain in the eyeballs in 7. The remaining 6 complained of scotoma. In both those with and those without goitre, the eye symptoms dependent upon migraine are here excluded.

10. *Affections of smell.*—The sense of smell is spoken of as sometimes affected. It was completely lost in one of my cases with goitre, and lasted for a number of months, to return again on her recovery from the disease.

11. *Pains.*—Among the prominent symptoms of Graves' Disease are pains of great variety as to their seat and nature, for they are both general and local in their distribution; but, nevertheless, they usually present some features in common which render them characteristic of this malady. Some of these pains are characteristic on account of the parts implicated, as the palms of the hands, the tips of the fingers, or the tips of the toes and heels. In one case without goitre the palms of the hands were extremely painful. Pains in the tips of the fingers were

noted in 6 cases with goitre, and in 5 cases without goitre. In the toes, in two cases with goitre, and in 3 cases without goitre. Pains in the heels were noted in one case with goitre, and in 5 cases without goitre. They were all characterized by sensitiveness to pressure, like the tenderness of the external ears already mentioned; and in those in whom the heels were involved, walking was rendered difficult. The tenderness, however, in all cases seemed to be very superficial, and not even when in the heels could it be termed articular, for the ankle joint could be freely moved without pain.

True muscular pains, on the other hand, are very frequent, and in patients without goitre are often mistaken for rheumatism, as the affected muscles become stiff and painful on movement. They differ from rheumatism in the muscles implicated not being painful on firm palpation, show no heat or swelling, are not affected by changes in the weather; and moreover, the pains are very shifting, appearing and disappearing much more rapidly than do rheumatic pains, and very commonly are better in the evening than in the morning. Unlike muscular rheumatism, they rarely are referred to the back. One of the commonest sites is in the muscles of the neck, particularly in the sternomastoid and the upper division of the trapezius. The left side of the neck is affected about twice as often as the right, having been noted in 7 cases with goitre on the left, and in 5 cases with goitre on the right; and in 3 cases with goitre on both sides. While in the cases without goitre, they occurred in 5 patients on the left; in 2 on the right; and in one on both sides.

These pains, moreover, may affect the muscles of both the upper and lower extremities quite extensively. In one case for two years before goitre developed in a lady, she was greatly annoyed with nocturnal pains in the anterior aspect of both thighs; and the same kind of pains occurred in one case without goitre. These pains could all be distinguished from peripheral neuritis by their transient character, and from true neuralgic pains by tenderness to pressure and by their causing muscular stiffness. In a few instances, the joints—especially the wrists, knees and ankles—became painful, when the differentiation from rheumatism became more difficult; and it is only the presence of other

symptoms of Graves' Disease which serves to distinguish them. From gouty arthritis they can be distinguished by the absence of the painful points on the condyles, which I have shown in a published paper[1] to be diagnostic of gouty inflammation.

12. *Headaches.*—Among the commonest sensory disturbances of Graves' Disease are headaches. With many patients they are almost of daily occurrence, particularly in the morning. I was early struck with their migrainous character, especially as they were so commonly accompanied with nausea, or other gastric disturbance. This was further borne out by the functional derangements of the eyes which, though not assuming the definite teicopsia of migraine, yet flashes of light, dark and bright colored spectra, and pain in the eyes are frequently mentioned. They differ from typical attacks of migraine in not coming on in severe paroxysms, followed by complete cessation for more or less prolonged periods, and they rarely lead to vomiting. In other respects they so resemble migraine, that finally I was led to ask if the patients themselves had suffered from migraine previously to the development of Graves' Disease, and whether they had migrainous relatives. The results of these enquiries were interesting. Out of the list of 36 with goitre who were questioned, 19 had suffered from migraine in previous years, 11 of them severely. Particulars as to relatives are noted in 14. One (a man) had suffered greatly from migraine from boyhood, and so did his father. The rest were women. One had a mother and sister who had goitre, and they, with three other sisters and a brother, were martyrs to sick headaches. Another had an aunt and a cousin on her mother's side who had goitre, and they, with her mother's whole family, were migrainous; but not her father's. Another, her mother and brother; two had each a migrainous sister; one a father very severely affected; one a father and a sister; and one a mother and sister.

Of the remaining 12, two men and 9 women, none were much troubled with headaches. One, however, had a mother who also had goitre, and who had migraine badly. Another also had a mother with goitre, but in her case and in three other patients no fam-

[1] Transactions of the American Association of Physicians, Washington, Vol. xi., 1896.

ily history of migraine could be elicited. Among the 28 cases without goitre, 18 cases are noted with headaches, seven had suffered from migraine, and three had no headaches at all. Flashes of light and scotoma were mentioned in four cases with goitre; and mentioned in eight cases of the patients without goitre. One woman without goitre after the disease developed, when she was 42 years of age, had headaches for the first time, and often attacks of blindness in the right eye. She had a sister who had goitre and who was very migrainous. Her mother, who suffered greatly from migraine, finally died of a disease whose nature neither of her physicians (who were eminent New York practitioners) could diagnose; but which both this patient and her goitrous sister were now sure resembled their own malady. As to relatives, particulars were obtained in eight of the cases without goitre. Four (one man and three women) had each a sister with goitre who also suffered from migraine. One had a mother and two brothers who suffered from migraine, but her two sisters did not. One had a migrainous mother, but her three sisters were free. One (a man) had a mother, a sister and two brothers who had migraine. Two themselves had migraine, but there was none in their families. This frequent association cannot be merely a coincidence; and as we shall see, is not without its bearing upon the pathology of Graves' Disease.

13. *Vertigo.*—Vertigo is an occasional symptom and was pronounced in five patients with goitre, and in five patients without goitre. Though it might be expected to be connected with gastric derangement, yet I found it almost uniformly presenting the characters of aural vertigo instead, being most pronounced in patients who suffered from tinnitus or loss of hearing. When severe, it had the character of aural vertigo in causing a great sense of fright. The worst example of the kind occurred in a patient without goitre, who entirely lost her hearing in the left ear, until she recovered from her disease, when the hearing returned and the vertigo ceased. In no one of the cases in whom abasia occurred was vertigo complained of.

14. *Parœsthesiæ.*—As might be expected in a disease with so many nervous symptoms, various forms of paræthesiæ are common. Of these, tingling and numbness are the most frequent

and usually more pronounced in the lower than in the upper extremities. Of 42 patients with goitre, 10 complained of paræsthesiæ. It is noticeable that numbness and tingling were frequently associated in time with headaches, thus bearing out the resemblance with severe migraine, in which these symptoms are likewise common.

Digestive Disturbances.—Much the most serious derangements in Graves' Disease, for their effect upon the nutrition of the body, are those connected with the functions of the alimentary canal. It may be said that Graves' Disease increases in severity and becomes dangerous to life in direct proportion to the degree in which the gastro-intestinal tract is involved. None of the other derangements, not even the tachycardia, and least of all the size of the goitre, seem so to tell upon the general health of the patient as the diseased condition of the stomach and intestines. The bearing of this important element upon the pathology itself of Graves' Disease, as well as upon its successful treatment, will be discussed later.

The first fact to note about the digestive disorders of Graves' Disease is that they are specific in their characters, and distinctively unlike other affections of the gastro-intestinal tract. In contrast to the variety in the symptoms of ordinary digestive derangements in different persons, the gastro-intestinal disorders of Graves' Disease are almost uniformly similar in their chief features, however the other symptoms of the complaint may vary between different individuals. Thus, from their earliest development to their end, in fatal cases with uncontrollable vomiting and diarrhœa, they never present the character of inflammatory, or of ulcerative, or of exudative processes. Moreover, whether in their slighter or in their severer forms, they are not amenable to the ordinary remedies prescribed for digestive disorders, thus confirming the inference that they are peculiar in their dependence upon this specific malady. The most significant fact, however, about them is that with rare exceptions they develop, not during the course of the other derangements, but much before them. If careful enquiry on this subject be made, it is striking to find how generally the patients admit the

presence of digestive symptoms often for long periods before any of their other derangements.

Out of the entire list of my cases of both forms, only four patients (two with goitre and two without) stated that they previously had suffered from no trouble of either stomach or bowels. Two of these patients (one with goitre and one without) subsequently had attacks of apparently causeless diarrhœa. With two of my cases, both without goitre, their digestive troubles began so suddenly that they could give the exact date of their occurrence. In the great majority, however, of both classes the story of their derangements was much the same throughout, as if the symptoms always remained the same in kind from the first, and not like the relapsing or changing forms of ordinary gastro-intestinal affections.

15. *Characteristic disorders of the stomach.*—Thus, as to the stomach, at no time is there any tenderness on palpation, or any epigastric rigidity, as in conditions of gastritis, ulcerative or otherwise. With a number of my patients gastric lavage had been employed for relief of the symptoms, but the uniform report was that no mucus was found in any amount in the outflow, nor did the lavage afford relief. A common symptom was nausea which, however, but rarely led to vomiting, except in advanced cases. This nausea was sometimes extremely persistent, in one case without goitre continuing fully two years before the tachycardia and the other derangements of the disease developed, as they did afterwards to an alarming extent. This nausea usually has no relation to the time of eating, occurring as often with an empty stomach as after meals. A much more common symptom is gastric flatulence which may persist, even after gastric discomfort has subsided, but ordinarily it constitutes one of the most annoying accompaniments of the complaint. The patients may attempt to relieve it by eructations, but uniformly deny that any acid or acrid sensation is produced in the throat or mouth, if they succeed in the attempt. Instead of pain or a sense of weight, or of cramps, they ordinarily describe their sensations as consisting of an ill-defined discomfort referred to the stomach, which with many is very distressing.

In my list of 42 cases with goitre, 7 complained of frequent

nausea; it was absent in 25, and not noted in 9. Among the 28 cases without goitre, nausea was present in 14 cases; absent or not noted in 14. Flatulence and gastric discomfort were present in 23 cases with goitre, and precisely the same symptoms were present in 21 cases without goitre.

16. *Characteristic disorders of the intestines.*—Intestinal derangements, on the other hand, are not only both frequent and pronounced in Graves' Disease, but they also seem to hold a fairly constant relation to the other characteristic symptoms. This is particularly true of the tachycardia, the nervousness, and the tremors, which are often aggravated with each exacerbation of the bowel derangement. Several patients asserted that attacks of nocturnal palpitation occurred only when the bowels became loose. The immediate reduction of the pulse rate, as we shall see, by certain forms of intestinal medication, would also appear to confirm this surmise. A sense of diffused distress throughout the abdomen, accompanied with flatulence, is even more common than the like symptoms just described in the stomach. With some this sensation is aggravated with every movement of the bowels, occasionally even when the movement seems to be regular and natural. The most charactristic symptom, however, is diarrhœa.

It was present in 25 of the patients with goitre; and in 13 of those without. It was present in all four of the fatal cases, becoming uncontrollable in each one. The diarrhœa of Graves' Disease is as peculiar in its way as any other of the accompaniments of the affection. Its exciting causes are usually difficult to determine, for though indiscretions in diet can be occasionally adduced, yet its onset seems often without any known reason. The only exception to this statement in my patients was that the indulgence in red meats, especially beef, was very commonly followed by a return of the diarrhœa, in those who had been free from it after leaving off meats. The commonest time of onset is the latter part of the night or early morning, occurring irregularly afterwards during the day, and not particularly apt to follow directly upon meals. The discharges are rarely preceded or followed by pain; are not usually offensive, but are watery and devoid of either blood, mucus or pus. According to

my experience, so long as the diarrhœa persists, no headway is made in the treatment of Graves' Disease.

On the other hand, a certain percentage of patients with Graves' Disease never have diarrhœa, but constipation instead. This was noted as habitual in 6 cases with goitre, and in 10 cases without goitre. Among these patients, however, 7 with goitre and 4 without goitre had occasional attacks of diarrhœa alternating with constipation. In every instance, their diarrhœa was stated to have occurred without any imaginable cause, and it was both painless and watery. In the cases with constipation, flatulence and a sense of discomfort was noted in 2 cases with goitre, and in 8 out of the 10 cases without goitre. In 11 cases with goitre, and in 6 cases without goitre, the bowels were stated to be regular and normal in the movements. In all of these, however, the other symptoms of the complaint were moderate, and the disease was only in a mild form or in an incipient stage.

17. *Bulimia.*—Bulimia, or a sense of intense hunger, is mentioned among the symptoms of this complaint. It was very marked in 6 of my patients with goitre (two men and the others women), in one of the latter preceding the goitre by more than two years, as did in her case all the other symptoms, tachycardia, tremors, pains, etc. The commonest time for its onset was in the night. The same symptom was present in 5 cases without goitre.

18. *Emaciation.*—Emaciation is a very noticeable symptom in the severe cases of this disease. As a rule, it is most pronounced in the patients who have suffered most from diarrhœa. One of the worst cases, however, among my patients was a woman who never had goitre or diarrhœa. She had to be padded to prevent the bones from cutting through the skin. She recovered wholly in time, and regained not only her full weight, but her physical strength and lived an active life for over four years, when she had an acute relapse and died suddenly from syncope. Emaciation was very pronounced in 17 with goitre, and in 6 of the cases without goitre.

19. *Insomnia.*—Among the frequent complaints of Graves' Disease is insomnia. We might naturally expect it to be from

the extreme nervousness to which many of these patients are subject; but I am inclined to ascribe it more to their digestive derangements, as it has all the characteristics of the sleeplessness of chronic dyspeptics. Thus, the majority are more troubled with wakefulness after midnight than before, and often in proportion to the disturbance of the stomach and bowels. This insomnia is also but little relieved by soporific drugs, and improves only as the digestive disorders improve. Insomnia was especially complained of by 21 patients with goitre, and by 18 patients without goitre. In all cases in which the insomnia was pronounced, the morning mental depression was naturally aggravated.

20. *Loss of hair.*—Falling out of the hair is often an early symptom, and naturally more noticeable among women. They are, therefore, very certain of its occurrence and of its date compared with that of other symptoms. It was noted in 21 cases with goitre, and in 6 cases without goitre. In one case it included the eyebrows. The loss of hair is not permanent, for it soon grows again with the first signs of general improvement. In all respects it resembles the loss of hair after prolonged fevers, like typhoid, and indicates, therefore, a profound and general toxæmia which involves every process of nutrition. One patient with goitre stated that when the symptoms of acute Graves' Disease developed upon a chronic goitre of 35 years' standing, her hair instead of falling out turned gray, and then returned to its normal color when the acute symptoms subsided.

21. *Pigmentation of the skin.*—Pigmentation of the skin frequently occurs in brownish-colored and discrete patches, but though classed by a number of writers as a distinctive symptom of Graves' Disease, I regard it as merely a sign of impaired nutrition, for it is quite similar to the discolorations met with in many wasting diseases and in chronic anæmics. Its hue also varies, in some resembling the bronzing of Addison's Disease. Its duration also is very variable.

22. *Itching.*—Itching of the skin, on the other hand, is quite characteristic of this complaint, more especially in severe cases. Like all other symptoms of Graves' Disease, it has no connection with inflammation, being accompanied with neither redness nor

eruption. It is apt to be most troublesome at night, increasing the insomnia by its stinging and yet shifting character. Scratching neither relieves nor aggravates it. It was noted in 13 cases with goitre, and in 5 cases without goitre. In no case among the women was it associated with pruitus vulvæ.

23. *Sweating.*—Sweating is a frequent symptom, and not always either nocturnal or indicative of an advanced condition of debility, for in some patients it occurred quite early in the complaint, before they had become much reduced. As in other conditions of idriosis, it was very variable, coming and going without any imaginable reason, but in no case preceded by fever. In my lists troublesome sweating was recorded in 7 of the goitrous cases, and in 4 of the non-goitrous cases.

24. *Vestical irritability.*—Irritability of the urinary bladder, causing frequent micturtion, is a very common and troublesome complication, especially as it is more apt to occur at night and thus aggravate the insomnia and nervousness of the patient. In full keeping with the other symptoms of Graves' Disease, it has no connection with inflammation, and hence never presents the accompaniments of cystitis, the urine being free from mucus and pus. It was noted in 14 of the cases with goitre, and in 10 of the cases without goitre.

25. *All symptoms worse in the morning.*—If it be asked, what are the most peculiar or characteristic clinical features in Graves' Disease, I would answer that next to its specific tachycardia is the morning exacerbation of its chief symptoms. No careful observer can fail to be struck by this singular phenomenon. In my notes, out of the 42 cases with goitre, only 4 denied that they were worse in the mornings; and it is doubtful if one of these, an Armenian woman who could not speak English, understood the question. On the other hand, the remaining patients had no hesitation in admitting that they were always worse in the morning, and better in the evening; and this statement is quite as distinctly present in the histories of the patients who never showed any change in the thyroid gland. Thus, of these 28 cases, morning aggravation was well marked in 25, and denied in only 3; and of each of these it might be correctly stated that the disease was still in an incipient stage. This characteristic

of the disease is all the more exemplified when we pass from general conditions to particular symptoms.

Thus as to the one symptom of muscular tremor. In no less than 6 patients with goitre, and 3 patients without goitre, it was recorded that the shaking of the right hand prevented their writing in the forenoon, so that they had to wait till evening before they could hold a pen. One patient without goitre, not being accustomed to write at all, yet said that she could not sew in the morning, but could do so in the evening. But all other leading symptoms share likewise in this curious diurnal variation. Thus the tachycardia, instead of being lessened by the night's bodily rest, is almost always increased in the early morning, compared with the previous evening. The commonest time for palpitation is also towards morning. The headaches, as might be expected from their migrainous affinities, are far more common mornings, and worse in their onset, and in average cases they subside towards evening. Perhaps the most marked in their morning visitations are the periods of mental depression. Men, quite as much as women, will complain of their waking with a heavy weight on their spirits, and with a beclouding of the mind wholly precluding any mental effort or concentration of thought, and then feel more like themselves in the afternoon. Those also who suffer from insomnia often find that they can go to sleep readily, but after midnight they grow obstinately wakeful.

It is, however, with patients who have diarrhœa that this complication is the most uniformly worse as morning approaches. The first onset of this symptom also in those who before have been free is scarcely ever in the daytime, but in the early morning. When diarrhœa occurs, it is noteworthy how along with it increased tachycardia, palpitation and nervous depression occur, and too uniformly to doubt that at this period there must supervene a marked increase in the specific toxæmia of the disease. An analogous aggravation of symptoms in the early morning is common in melancholia, and in those ill-defined nervous derangements now classed under the elastic term "neurasthenia." But in melancholia this feature is by no means so uniform as in Graves' Disease, while I do not doubt that many cases

of so-called "neurasthenia" are really examples of unrecognized Graves' Disease. This morning element can only be ascribed to derangements in vital chemistry; but whether that can be explained by the increased activity of the thyroid gland after midnight will be discussed under the head of pathology.

26. *Disease chronic.*—There is one element in Graves' Disease which, when duly considered, fully demonstrates its distinct and specific nature, and that is its chronicity. With all its multitudinous developments in deranged functions, it remains the same throughout a long course, and never merges into anything else. All its chief symptoms preserve the same characteristics however long they persist. Thus, its tachycardia continues through months and years as no other tachycardia ever does, with meantime surprisingly little change of any other kind in the over-acting organ. But the tachycardia is not an isolated phenomenon in Graves' Disease. Instead, it is uniformly accompanied by a characteristic train of other symptoms which are as much part of the malady as it is, and which also continue with little variation or little modification. The gastric derangement never becomes a gastritis, nor the diarrhœa an enteritis or a colitis.

My own experience leads me, therefore, to hesitate in pronouncing any patient to be cured, who has once had Graves' Disease fully developed, until a long time has elapsed after apparent recovery. Instead, I always tell patients that they must expect to keep up their treatment for at least two years before they can be sure of complete recovery. On that account, I am skeptical of some reported rapid cures after certain procedures, especially surgical ones, as I want to know more of the after history of the patients. A certain proportion improve, or even recover, spontaneously; but I have found that relapses are common, sometimes after intervals of years. Most of the observations which I have read on this disease are based upon the clinical histories of hospital patients, not many of them extending beyond a few months, whereas two years is not too long, and one year is not enough, for a satisfactory history.

One reason for referring to the chronic course of Graves' Disease is that this of itself shows that it is no passing ailment, which might give opportunities for mistakes in diagnosis. Who

ever has a complaint with always the same symptoms for two or three years ought by that time to have his trouble recognized as the same, and not as something else, even if we cannot give it a name. And it is just because those cases without exophthalmic goitre are not a whit different in this feature of chronicity from those with goitre that they must be classed as true cases of Graves' Disease. It is no more justifiable to apply the terms incomplete, or latent, or abortive, to them, when the patients suffer severely for months together from the characteristic derangements of the disease, than it would be to designate a case of phthisis as latent or incomplete because throughout the long course there was entire absence of hemoptysis.

As with other chronic maladies, however, cases do occur of acute Graves' Disease. Thus, as already mentioned, two of my patients without goitre could fix the exact day on which the trouble suddenly began. One in my list of cases with fully developed goitre, whom I saw in consultation, gave a history of only five weeks' illness; another who developed dangerous acute symptoms had been ill only two months, and there are numerous instances reported of the sudden development of exophthalmic goitre. Still, acute Graves' Disease is a rarity, the rule being that it begins imperceptibly, and continues indefinitely as to time, but most definitely otherwise, in the progressive development of a long array of derangements which are peculiarly its own.

27. *Family complaint.*—One of the most conclusive evidences of the identity of the disease in the non-goitrous with the goitrous patients on my list is their equal share in the occurrence of Graves' Disease with goitre among their relatives. That Graves' Disease is a family complaint has long been known. Thus, in my list of 42 patients with goitre, 6 had relatives who were subject to this complaint. But turning for comparison to my patients without goitre, 6 had relatives who had goitre. This percentage among them of family liability to Graves' Disease certainly cannot be ascribed to coincidence, particularly as Graves' Disease (quite unlike phthisis) is not a common affection in any community. I may add that I have been particular to enquire whether it was Graves' goitre, and not

other forms of goitre, which the relatives had. The value of this element in proving that the non-goitrous cases had Graves' Disease is sufficiently shown in the enumeration of the instances noted in the records.

28. *Death sudden.*—In fatal cases, the terminal symptoms of Graves' Disease are as characteristic as those of the preceding stages. If the patient be lying in bed, the persistent tachycardia changes to extreme irregularity of the pulse in frequency and in size, becoming often uncountable in rapidity, then thready, then intermittent, and sometimes apparently slow from failure of the cardiac systole to reach the radial. Then it suddenly stops and all is over, without a struggle. If the patient be sitting up, as they often do then in spite of remonstrances, the end comes in the same sudden but quiet fashion.

Previous to this, however, the story of the antecedent symptoms is remarkably uniform. Their nervousness has increased to a distressing restlessness. Delirium sometimes resembling mania sets in, and with it an obstinate refusal to accede to the recommendations of their friends, particularly in refusing to take remedies. The most common precursor, however, is the supervention of persistent vomiting and diarrhœa. As disturbances of the gastro-intestinal tract always hold the first place in their serious effect upon the strength and nutrition of patients with Graves' Disease, so it is due directly to their becoming uncontrollable that death ends the scene. But as will be seen presently, this clinical picture is substantially the same in my two fatal cases with goitre and in the two without goitre.

CLINICAL HISTORIES OF CASES WITH GOITRE.

CASE I.—Mrs. M. Æt. 50. Widow.

The particulars of this patient's history are given in the detailed description of Case I, of the section on Fatal Cases.

CASE II.—Miss M. W. Æt. 50. Unmarried.

Her notes in my case books are:

December 9, 1893: Usually enjoyed good health, except occasional attacks of gall stone colic. First consulted me for trembling of the right hand, sometimes of the lower lip. She is also troubled with throbbing tinnitus in the left ear, especially on lying down. December 21: Constant throbbing in the left ear, with every day a sense of general weariness.

January 6, 1894: Tremor extended to muscles of the face; has a feeling of stiffness in her muscles at night. Also has a sense of intense hunger coming on in the night. January 25: Great complaint of a sense of fatigue; throbbing in the ear almost drives her to distraction; has periodical pains in front of the thighs, quite severe, coming on at night. Tongue tremulous; sensible of inward tremors all over. Good deal troubled with insomnia. January 31: Almost distracted with throbbing in the ears. Pains in face better. February 18: Depressed in spirits, with a sense of nervous prostration. Sleep very poor. Tremors increasing, in her tongue, in her face, and in her right arm. Had to leave all letters till the latter part of the day, when her hand seems to become steady. Insomnia extreme. Pain in thighs has returned at night. March 17: Insomnia better. Still has sudden attacks of exhaustion in the day, without apparent reason. April 7: Tinnitus continues. May 10: Insomnia better; not so exhausted. Tinnitus better, though continuous; but she has pains in the right forefinger. Muscles of the right hand tremble, with jerking in the tendons, like clonus. (Knee jerks much exaggerated.) Begins to have severe headaches, most on waking; better at night. May 25: Tremors increasing. Complains of almost continuous headaches. Had a slight epistaxis once, a new symptom. Now has a complete anosmia, which has been coming on for some months. Pulse 120. Temperature normal. October 11: Better after vacation in the country. Has some headaches; pain in the right eye. No epistaxis. Tremor in the right hand less. Pains in thighs less,

but a sense of soreness there. Insomnia continues; but she says she can distinguish flavors. Complains now of vesical irritability. Pulse 116.

February 18, 1895: Been doing fairly well since last October. Roaring left ear returned. Insomnia continues. Pains in thighs come on when she lies down. To-day had an attack of slight nose-bleeding. Pulse 114. March 5: Better, but complains of pain in back. Much troubled with flatulence. Headache, affecting the right eye. November 25: Troubled with palpitation, and can count her heart from throbbing in her ears. Old pain in front of thighs at night again. Has tremor and right hand shaking again. December 4: Throbbing in head continues. Pulse 124. December 29: Violent headache, over accustomed right eye. This time with vomiting. December 26: On morning of 27th, so violently as to cause her to cry out.

January 17, 1896: Attacks of headache, which the ergot relieved in one dose; but she was sick at the stomach for three days. Since then has had attacks of numbness in one ear, with pareses of left leg for some hours. Return of gastric dyspepsia. January 27: Headaches nearly every day. Pains and throbbing in ears as bad as ever. Pulse 110. February 11: Violent headaches return, always controlled by the ergot. Still complains of same noises in ears. Now has retinal images when closing the eyes. Pulse 118. February 25: Much better. Pulse 130. Headaches very slight. March 10: Pain in right shoulder. Throbbing in ears continues, and old pain in thighs. Pulse down to 86. March 17: Goitre at last! First appearance of enlargement of the thyroid gland on my visit to-day. The enlargement is uniform, and Stellwag's symptom is present. Meanwhile all the other symptoms are improving, especially the tachycardia. July 14: The goitre still remains, but constantly varies in size. The noctural neuralgias and the tremor have almost disappeared; but what she most appreciates is that her ear symptoms have ceased.

April 28, 1898: Since last date she has been doing very well. Goitre gradually disappeared altogther. Distracting noise in her ears much better; but she thinks if she leaves off the capsules, which she has been taking since April, 1896, she is threatened with a return of them. Tremor all gone.

CASE III.—Mrs. W. G. Æt. 48.

This case I was consulted about in 1886, but not being my own patient, I am able to give account only of her leading symptoms. She was naturally of a very lively disposition, and very fond of the engagements of society, which her wealth and station allowed her fully to enjoy. She had always been in good health,

when for no imaginable reason she found that she was becoming extremely nervous. Obstinate painless diarrhœa then set in, and with this continuous rapid action of the heart. Her physician found a loud systolic mitral murmur, and as edema of the feet soon followed, he told the family that she had serious heart disease. She soon became alarmingly prostrated, very insomnic, and her voice almost left her. She had tremors, both general and in the hands. I gave my opinion then that she had Graves' Disease, which was soon afterwards confirmed by a rapidly developing goitre, with exophthalmos, and with both Græf's and Stellwag's symptoms. She continued to lose flesh and color for two years, and she had frequent sudden falls when walking. Under treatment for Graves' Disease, she gradually improved until both the goitre and the exophthalmos have wholly disappeared; and now, after a lapse of fourteen years, she enjoys very fair health.

CASE IV.—Mrs. A. G. Æt. 40.

This patient I have attended for a number of years, her most persistent trouble being attacks of severe migraine. She is a very accomplished lady, and prominent in both social and public engagements, in which she frequently over-taxes herself, with returns of her prostrating headaches as a consequence.

In the spring of 1890, after a prolonged visitation of migraine, she noticed that her heart was beating very fast; that she was changing (as she expressed it) into a weak, trembling, nervous creature, lacking all the repose of strength. Her symptoms were, besides the tachycardia, 120-130, tremors, wandering rheumatoid pains, great muscular weakness, loss of flesh and persistent flatulence, with a sense of distress in the stomach. This was followed by goitre, most pronounced on the right side, but with nothing unnatural about the eyes. She had suffered when a child from both rheumatism and chorea; and she has two daughters who each in their tenth year I treated for chorea. Under treatment for Graves' Disease, the goitre disappeared in 1891, and has not returned since.

CASE V.—Mrs. W. Æt. 65.

This patient has always enjoyed fair health till she was 65 years of age, when she began to be very dyspeptic, with gastric flatulence, accompanied by extreme nervousness. After several months of these symptoms, along with insomnia, her thyroid began to enlarge, mostly on the right side. She also had a slight protrusion of the eyes, and the Stellwag symptom. Tachycardia persisted for two years, and often at night she had respiratory crises, resembling the laryngeal crises of tabes. For some months

she had frequent recurrent albuminuria. She wholly recovered from her symptoms, the goitre entirely disappearing, and she remained in good health for four years, finally dying from pneumonia during the influenza epidemic of 1891. She had a marked family history of rheumatism.

This lady had a daughter, however, who lived till she died at 36 years of age from myxedema. Her first symptoms began with an enlargement of the uterus, which attained a great size, and post mortem seemed like a softened mass of tissue infiltrated with mucus. She showed no other signs about her face, extremities or body, of myxedematous infiltration; but she became very enfeebled in mind, as well as body, with frequent movements of the jaw of a choreic character. Her pulse was very slow and weak, and her general condition was the exact reverse of Graves' Disease. The thyroid gland was wholly atrophied, and she died comatose. Her case is of interest as one of cachexia thyroidprevia in the daughter and Graves' Disease in the mother.

CASE VI.—Mrs. D. Æt. about 35.

April 3, 1899: I treated her ten years ago for goitre, but with no exophthalmos. She was once pregnant, giving birth to a child at term which, however, lived but a few hours. She improved in all her symptoms, except that the goitre did not disappear. She comes now with all the general symptoms again, but no pains. The goitre is about one-half the former size. Pulse 108. She is a good deal troubled with migraine and with tremors; occasional palpitation; also much flatulence and constipation. April 29: She is always worse in the mornings. Continual throbbing in her ears. June 30: Very much better. Headaches and throbbing in her ears gone. Some pains in the left leg.

CASE VII.—Mr. T. Sick two years before treatment.

This case is of interest on account of the advanced stage of the disease before the treatment which I recommend was begun. Dr. J. C. Thompson, of Pittsburgh, Pa., having read my article which had been copied in the *American Ophthalmological Journal,* wrote to me that he had a brother who was suffering from Graves' Disease, and asked for some further particulars about the treatment. I answered his letter accordingly in November, 1893, but not hearing any further about the case, I wrote in March, 1896, to ask if he had tried the treatment, and with what results.

I append his reply in full, as a corroboration from an inde-

pendent witness of the good results which I have found in practice from dealing with this affection as primarily due to the absorption of intestinal ptomaines.

"524 Penn Avenue, Pittsburgh, Pa.,
"March 9, 1896.

"My brother at the time I wrote you had had the disease two years, having lived in Helena, Montana, at an altitude of four thousand five hundred feet above sea level, for most of the time. Some two months before I corresponded with you he had returned to his home in this city for treatment, being thoroughly broken down. His Helena physician thought he would not live a week longer if he remained in that city. On his return he went under treatment instituted by myself and also two other physicians of eminence in the regular profession. His weight had fallen off from 165 pounds to 125 pounds; his pulse varied from 130 to 150; the thyroid gland on the right side was greatly enlarged; he perspired copiously on the slightest exertion; the hands trembled; the breathing was labored and audible; the voice weak and husky; his bowels were loose, there being five or six movements in twenty-four hours, and in connection with this condition he had a ravenous appetite; he was compelled to void urine three or four times a night; had an unnatural gayety of manner, and, in brief, presented a perfect clinical picture of a typical case of Graves' Disease. Under the treatment suggested by the two physicians spoken of and by myself, which consisted of heart sedatives and 'tissue builders,' he went from bad to worse steadily, until his weight was not over 100 pounds and he could scarcely stand up. At this time I heard of the results secured by an eminent gentleman in New York, Dr. Rockwell, by the use of electricity in the disease (published in the *Medical Record*), and as a last extremity took my brother on to see this gentleman. He gave a guarded prognosis, and thought I had better take my brother home, which advice I followed. After this there was a rapid and constant decline in the condition of the patient, and none of the physicians who saw him thought there was any hope of his recovery. At this time I read the article you had written and commenced the line of treatment at once. In my notes, taken at the time, I found that the following was the condition of the patient the evening before the dose of calomel was given, preliminary to the treatment to follow. Pulse at 8 P.M. 146; respirations, 30; temperature, 98°. Following the dose of calomel the pulse dropped to 104 the next morning, the lowest it had been since I had seen the case. The line of diet suggested by you

in your article and letter was strictly followed, and an immediate and unmistakable improvement in all the symptoms followed. This was continuous, so that at the end of two months there was a gain of twenty pounds in weight; and at the end of six months a gain of 46 pounds; and corresponding improvement in all the other features of the case. The pulse generally remained about 104 to 110. At the end of six months the patient then went to Southern California to escape the severe winter here; but, not having the chance to get the diet regularly, he did not improve much there. After a residence of five months there he returned here, and has continued the diet and treatment without variation or cessation ever since, so that at the end of two years and a half his condition, as represented by general signs, is: March 6th: Pulse, after exercise, 90; respirations, 22; temperature, normal; weight, 146 pounds; bowels regular, one movement in twenty-four hours, and normal; skin congested about the ears and neck, but natural otherwise; appetite good; sleeps well; has no pains; wants to go into business; eyes still unduly prominent, but not so much exophthalmia as formerly. The von Græf sign absent, except when excited. The thyroid enlargement is as great as ever; is comparatively strong; walked six miles the other day without fatigue. He is satisfied to continue the diet and treatment indefinitely, feeling certain that his life was saved by the treatment, as I do and all the other physicians who saw him."

CASE VIII.—Miss L. W. Æt. 35. Public school teacher.

May 22, 1893: Called first. Her aspect was like one in the last stage of phthisis, as regards extreme emaciation and anæmia. Eyes somewhat prominent, but no von Græf's symptoms. Thyroid uniformly but not considerably enlarged. Hair much thinned; much tremor of the hands; voice tremulous and weak; abasia just beginning, as she had had her first fall that day. Heart action tumultuous, but without murmur. Pulse 152. Has been greatly troubled with diarrhœa for nearly two years, and latterly with much bladder irritability, also itching of the skin and persistent insomnia. Meantime she has become so weak that she feels as if she might die at any moment. The patient was with difficulty removed to her father's house in the country, where she followed out the line of treatment recommended. July 19: A letter from her mother states that she is greatly improved from the dying condition she seemed in upon her arrival at home. Her diarrhœa is checked, and her sleep is much better. August 19: The patient was able to write herself. Movement of the bowels still too frequent. November 17: Writes that she is steadily gaining in flesh and strength, but

that the goitre and exophthalmos still persist; bowels move three or four times a day, but the movements are not diarrhœal. The itching continues, but she sleeps well.

February 3, 22, and March 22, 1894: Slow but continued improvement, except that she has returns of old migrainous symptoms and the vesical irritability continues. May 18: She returned to the city to-day, and presents a striking contrast to her appearance a year before, being now quite full-faced, and with a natural healthy appearance, but for her moderate exophthalmos. Pulse 124, rather high tension. Bowels move twice a day, but are not loose. Had to have her hair cut, it was falling out so. June 29: Still feels that she is gaining; but pulse 126, high tension. Bowels, however, inclined to looseness if she modifies her diet at all. Itching still troublesome. September 22: Patient able to resume her duties at school. Looks well. Pulse 114. On August 2 had a bad fall, previously having for two days felt a weakness in the knees. Through October and November continued to hold her own in much the same condition.

January 5, 1895: Better, but cannot change her diet without having a return of her old symptoms. Through the winter attended well to her school duties. May 18: For the first time pulse down to 100. June 18: Gaining in flesh and strength. Pulse 88. Bowels now inclined to constipation. October 18: Has felt practically well all summer, and has resumed teaching.

February 22, 1896: Had some relapse of diarrhœa and rise in pulse, with return of bladder irritability from taking fruit. On resuming her milk diet and taking the medicines she was soon better again. June 20: Patient considers herself about well.

January 21, 1898: Pulse down to 76. She has, however, insomnia, tinnitus, looseness of the bowels and irritation of the bladder. Always benefited for a few days in all these symptoms by the blue pill. March 7: Pulse 64. Looks very well; but still troubled with vesical irritability, and with looseness at night. August 12: Still troubled with vesical irritability. September 9; Pulse 100. October 1: Has had to give up her work at school and is insomnic. December 1: First symptoms of melancholia. No symptoms of Graves' remaining. Goitre disappeared.

CASE IX.—Miss M. P. Æt. 23. Daughter of a wealthy manufacturer in Northern New York.

May 27, 1893: This patient first called in 1891, for tachycardia and moderate goitre, with mitral systolic murmur. Calls to-day, having been very much better, but the mitral murmur is still there. Pulse 108.

September 10, 1895. On the 7th, she was taken with a pain behind her left ear. The next day she first noticed that her face

was affected. Comes now with complete Bell's paralysis of the left side; cannot close the left eye. Tongue has a metallic taste. Says, that she had the other side of her face paralyzed in the same way five years ago. October 18: Paralysis slowly improving. Cannot close the eyelid. October 23: Slow improvement. Lower eyelid still immobile. October 28: Troubled with general nervousness. November 18: Nearly well.

January 25, 1896: Comes with only the raising of the lip now, when she closes the eye. Complains of frequent headache. Goitre gone.

May 1, 1897: Face now natural, but left corner of the mouth sometimes twitches. Tremor of the lids much more in the left; has some indications of her former troubles; insomnia, general nervousness, and fits of general depression. Palpitation after eating. September 29: Still troubled with palpitation after eating. Pulse 120. Insomnia better. November 23: About the same. Pulse 114. Once in a while has pain in the left ear.

February 12, 1898: Looking better generally, with no complaint, except nervousness and palpitation after eating. Pulse 108. April 23: Pulse 116. Feeling generally better. July 22: Has palpitation yet, sometimes it lasts all day. Still has pains behind her ears.

November 29, 1899: Has been feeling much better during the past year. But still has palpitation after meals. Pulse 102.

April 6, 1901: Has sudden attacks of palpitation at night.

March, 1903: This patient has so far fully recovered that she contracted marriage in 1902, and has now a healthy child.

CASE X.—Mr. Patrick S. Æt. 24. Gardener, son of healthy Irish parents.

April, 1894: First came under my treatment. Had always been healthy and of temperate habits. For no reason that he could account for he began to feel excessively nervous, tremulous, and troubled with insomnia and palpitation. He was also becoming prematurely bald, and so weak that he could hardly stand. Emaciation was also becoming very pronounced. Pulse 120 to 140. Moderate exophthalmos and very variable goitre. He improved greatly under treatment until October, 1894, when he had a severe relapse caused by emotion on the death of his mother. After that, by rest and being more attenive to his diet and treatment, he gained flesh again.

June, 1896: Present state, nearly well; still has some goitre.

CASE XI.—Mrs. B. Æt. 30. Wife of a physician.

February 13, 1896: Husband reports to me that I prescribed for her for Graves' Disease five years ago. She then had pronounced exophthalmos, but no thyroid enlargement, nor ever has

had any. She was ordered then to take fermented milk and scarcely any medicine. The tremor of the hands at that time was so great that she could not handle a tumbler of water. She lost her hair to a great degree, and she fell in weight from 130 pounds to 95 pounds. She has adhered mainly to this diet, and is now much better and has regained her normal weight. I found, however, that her pulse was 114, and so put her on intestinal antiseptics.

CASE XII.—Miss C. Æt. 35.

April 23, 1894: I treated this patient thirteen years ago for epilepsy then of three years' standing. She recovered in one year, with no recurrence to date. She has suffered from palpitation for a year past, with rapid heart action, and a sense of great prostration and muscular weakness; often being suddenly awakened, in the night, by the palpitation. Pulse 116. Slight enlargement of the thyroid on the right side; no exophthalmos; general tremor. May 7: Tendency to diarrhœa. Whenever this begins her heart is at once affected. May 23: Pulse down to 88. June 1: Pulse 110. Some diarrhœa, with tenesmus. June 20: Cramps in bowels, without diarrhœa. Continuation of prostration, and much general nervousness; has some symptoms like migraine. An attack of blindness, with numbness in the left arm, in the tongue and the nasal region, followed by severe headache. Throughout June these attacks occurred occasionally, each time accompanied with palpitation and nervousness. July 11: Feeling better, but still has tendency to diarrhœa. Pulse 104. October 7: Generally better, but attacks of diarrhœa. Pulse 94. November 12: Pulse 84. Generally better, but occasional diarrhœa, once after eating pears, had an attack of blindness and faintness. Goitre disappeared.

February 5, 1896: Feeling well. Pulse 78. Taking treatment regularly, and has no headaches. The connection between over action of the heart and intestinal derangement is particularly noticable in this case.

CASE XIII.—Miss Annie H. Æt. 18.

May 23, 1895: Delicate girl, looking quite anemic. Had lately been losing flesh, and was much troubled with loss of hair. Very nervous and weak, and inclined to frequent attacks of syncope. Pulse 124. June 3: Felt better and stronger, and had had only one "faint spell" since beginning treatment a week ago. Pulse 126. June 17: Better. Pulse 104. July 18: Feeling much improved. Pulse 100. Though this patient had neither exophthalmos nor goitre when she came on May 23d, during the past week the thyroid enlarged so for four days that she could not fasten her

collar about it, but in a few days it again wholly subsided. By September 1st her condition was so good that she ceased attendance, having gained in flesh and color. Pulse normal, 80.

CASE XIV.—Mrs. B. Æt. 55.

March 13, 1895: Three years ago she noticed that the thyroid began to enlarge. No exophthalmos. Has been very nervous, with rapid heart action. Weakness of the voice; weakness of the knees, though she has had no actual falling. Much tremor of hands, especially in the mornings. Has lost flesh and has grown worse, especially since taking thyroid tablets prescribed for her by a Boston physician. No cardiac murmur. Pulse 106. Had constant diarrhœa for four years before the thyroid enlarged. Has no diarrhœa now, but rather tends to constipation. June 8: Writes from Massachusetts that she is much improved. November 9: Much improved, but troubled with itching.

June 25, 1897: Feels a great deal better, but goitre persists. July 9: Doing well. December 18: Has gained in flesh and strength.

January 24, 1898: Goitre the same, and slight exophthalmos. Itching continues; much less tremor and much less nervousness. December 2: Pulse 120. Has fits of palpitation; but on the whole stronger, and looks better.

June 22, 1899: Says that in January she was recommended to give up the medicines on account of having the grip; returns now with the old symptoms aggravated, with increased tremor; loss of flesh from 148 pounds to 116 pounds; greatly troubled with bronchitic cough; pulse 130. June 30: Much better. Pulse 104, but intermittent. July 4: Improving, but still has some cough.

April 25, 1902: Better in many respects, but has become irregular in taking treatment. Now troubled with much flatulence in stomach, which causes palpitation and irritability. Feels generally stronger.

CASE XV.—Mrs. W. J. B. Æt. 40.

June 23, 1896: Three years ago, having previously enjoyed good health, she noticed that her heart was beating so fast she could not sleep. She then commenced to lose flesh. Was much troubled with constipation. Her hands would shake too much to pass a cup of tea at the table. Used to have long, thick hair; but it has come out frightfully. No special pains. Swelling of the legs from ankles to knees for three summers. This year from the hips. No kidney trouble. Has noticed enlargement of the thyroid. In January, 1896, protrusion of the left eye. Tremore very pronounced in the hands, especially in the right.

manner very excitable. Great throbbing in the ears. Pulse 100, some tension. Both legs edematous to the knees. Knee jerk diminished. Very nervous. No prostration; no vesical irritability; no itching. Heart strong impulse. Mitral regurgitation quite pronounced. Thyroid more enlarged on the right lobe; pulsations in it and the carotids very strong.

CASE XVI.—Mrs. W. Æt. about 35. Married eleven years, but never had children.

October 19, 1896: *Suddenly* in November, 1894, was taken with stomach trouble, with intractable vomiting, which would recur in turns of several days between two and three months. After becoming reduced in flesh from 135 pounds to 94 pounds, she noticed a rapid action of her heart. She has also suffered with diarrhœa, but most of the time from constipation. About a year ago her physician noticed that she had goitre, and that her eyes were becoming prominent. Has not lost hair on the head, which is very thick, but lost a good deal from both eyebrows and eyelids which, however, has grown again. She grew very weak, and is always fearful through weakness of the knees.

Sensory symptoms.—Pains like cramps in the right foot and calf, starting in the sole. Also "stitch" in sides of chest, and sometimes in the rectum. Much troubled with sweating. Intense itching all over the body, but not on the face. Has spells of irritability of the bladder. Courses stopped last winter from January to June. Patient complains of headaches just above the eyebrows. Pulse 124, high tension. Thyroid enlarged, especially the right lobe. Unmistakable exophthalmos. No von Græf; but eyelids when closed very tremulous. Tremor in the hands. Much troubled with insomnia; and feels much worse in the mornings. October 26: Feels much better. Less nervous; and for the first time in a good while free from headaches. Also friends notice that she talks less rapidly; used formerly to be difficult to understand. Also her fingers and hands do not move. She sleeps now without needing sulphonal. Pulse 116. Inclined to constipation.

January 2, 1897: Comes not so well; but this is explained by the dangerous illness of her husband, which has kept her up day and night. Pulse 135. January 9: Better, except that she is kept weak by attacks of cramps in the calves of her legs. Pulse 120. January 16: Comes feeling better in every way. Headaches gone. Strontium salicilate seems to have relieved the cramps at once. Pulse 114. Sleep practically good. General report better, but some palpitation yet. May 1: Out in the country and not so well. Palpitation and pulse increased, with morning headaches. June 4: Better. Headaches less; tremor

about the same. Weakness in the knees. Still the old cramps in the calves of the legs. Pulse 110. Sometimes a feeling of constriction in the throat. The goitre varies from time to time. Lids tremble but slightly. September 22: Stomach much improved. Now has morning headaches. Pains also in the eyes. Much insomnia and a good deal of vesical irritability. November 13: Considerable indigestion. Has gained 6 pounds in weight. Both goitre and exophthalmos diminished. December 18: Pulse 90. Thyroid enlargement constantly decreasing. Gained recently 7 pounds in weight. Headaches less; sweating stopped; occasional diarrhœa; vesical irritability continues; inward tremors, with sense of weakness. Pain in throat gone.

January 22, 1898: Looking much better; no headaches; no neuralgia; exophthalmos diminishing. Goitre almost gone. Pulse 114. Still has pains in the right foot. February 16: Improving; has had no more headaches. May 18: Favorable report; has gained 18 pounds in weight this winter. Pulse 85. July 8: Not so well again, from indiscretion in diet. September 25: Looks much better. Exophthalmos less and goitre diminished. Some pains in the eye balls. November 30: Not quite so well. Still has cramps in the calves.

January 16, 1899: Better in all particulars. Pulse 82. Goitre and exophthalmos still moderate. But has attacks of faintness. Still has cramps in calves. May 31: Improving. Pulse once down to 72. Cramps in legs better; but now for the first time complains of the legs being cold. May 17: Pulse down to 75. Goitre nearly disappeared. Cramps in foot continue. Some flatulence. Has gained 8 pounds in weight. Now weighs more than in 8 years. July 24: Favorable report in all respects, except slight flatulence. September 7: Still troubled with headaches, and foot still troublesome. Pulse 78. December 27: General improvement.

March 3, 1900: Better. Pain in foot gone. June 1: Writes that she has more morning headaches, and is very nervous. August 8: Has a relapse of all her old symptoms, with hard griping pains in the bowels after eating. Pains in the left ear and the left side of the neck and in the face, of a severe kind. October 6: Better; but still has morning headaches. December 17: Stomach troubles her, sometimes with vomiting and migrainous headaches.

January 7, 1901: Quite a favorable report. Feels stronger and head much improved. Stellwag symptom still marked. Some vesical irritability. June 14: Some rheumatoid pains in different parts. October 2: Bowels irregular, feeling great discomfort in them. December 23: Looking remarkably well;

eyes natural; goitre almost disappeared. Pulse only 68. Has none of her old symptoms, neither sensory nor otherwise.

CASE XVII.—Mrs. J. C. W. Æt. about 55. Widow, living in Boston.

May 1, 1897: Has had exophthalmos for eleven months, especially the right eye. Tachycardia. Pulse 110. Emaciation, lost 60 pounds; perspires a great deal; some itching; occasional vesical irritability; general nervousness, not natural to her temperament. Slight deafness in one ear. Used to have migraine, her mother also. Always feels worse in the mornings. Does not admit digestive derangement; no insomnia; no neuralgic symptoms; no weakness of the knees. Dates her trouble to a succession of domestic worries, by bereavement.

CASE XVIII.—Mr. P. R. S. Æt. 38. Clerk, in railroad office, at Mauch Chunk, Pa.

June 15, 1898: Tall, well-developed man, with dark complexion. Enjoyed good health, except for attacks of stomach trouble about three years ago, lasting about one year and a half. Six months ago noticed it coming back again. About seven weeks ago he began one day, after feeling some anxiety about some extra work, to notice that his heart began to palpitate. This palpitation has continued, with loss of flesh and tremulousness; has tremor of the hands, ruining his handwriting from being one of the best penmen in the county. Has tremor of the legs, weakness of the knees; much sweating; frontal headaches; stomach distended.

Examination: Slight enlargement of the right lobe of thyroid; no exophthalmos; no tremor of the lids; rheumatoid pains between the shoulders; no other pains; no loss of hair. Has been habitually constipated. Pulse 114. Manner agitated. Always worse in the mornings. Says every morning he has a swelling of the hands.

July 8: Better. Sleep better; is stronger; no longer losing weight; can write better in the afternoon. Pulse 106. Increase in rheumatoid pains. October 29: Not so much tremor in hands. Still complains of his pains. Has had diarrhœa for ten days, instead of constipation. Has lately been losing hair. With the diarrhœa lost 2 pounds. Became insomnic slightly. Goitre diminishing.

May, 1899: Much better.

CASE XIX.—Rev. J. M. Æt. about 45.

September 22, 1898: Was unaware of any heart symptoms, until suddenly a year ago was seized at 5 A. M. with severe pain

in the region of the heart, radiating into the left arm. Heart action then became very rapid, and has continued so. Had to stay in bed from nine to ten days with this, and for a number of weeks was too weak to go about. About six weeks after this attack began to notice a slight enlargement of the thyroid in the left lobe, which has continued ever since; no exophthalmos, but eyelids tremble.

On examination I find that he had tremor in the right hand for three years before the heart symptoms. Is sensible of general tremor. Has been for two years a chronic dyspeptic. Has had tinnitus in the left ear for two months. Has been a martyr to sick headaches all his life, with extreme nausea. Also his father. Pulse 98. Voice became very weak, and interfered with his preaching. October 5: Unfavorable report. Lost 6 pounds in weight since last report. October 19: On the whole better. Pulse 94. Tremor in the right hand continues. A good deal of insomnia. Complains of huskiness in his voice. November 3: Improved in every way. No headaches. Sleep better. Pulse 92. November 16: Continued improvement; voice much improved; gaining weight. Tremor in hand better. Pulse 84. December 19: Continued improvement. Much struck with the absence of headaches.

January 23, 1900. Pulse 80. Some increased tremor. March 8: Doing very well. Voice stronger, and can preach as he likes to; but tremor in hand continues. Much better at night. April 7: Steady improvement. Tremor in right hand better. As usual worse in the mornings. Has only had one headache in a year. Goitre the same. June 12: General improvement. Tremor in hand perceptible only in the mornings. No headaches. Goitre still the same. Voice all right. September 18: Steady improvement, but hand still trembles in the morning; but to his surprise gets better by using, and after preaching by considerable effort, becomes perfectly steady. November 20: Continued improvement. Pulse 80.

October 30, 1901: Practically well. Pulse 68. Goitre gone.

CASE XX.—Miss L. M. S. Æt. about 23.

October 6, 1898: Comes with general but moderate enlargement of the thyroid; slight widening of the palpebral fissure; tremor of the lids. Pulse 100. Duration only about eight months. Says she has not had any digestive trouble whatever. No nervous symptoms, either tremors or neuralgia, except sharp pain sometimes from right eye towards the ear.

June 27, 1899: Has continued treatment from last October. Eyelids still tremulous; goitre much diminished. Pulse 100.

July 7: Doing well, but some gastric disturbance. Pulse 95. August 7: Writes from Blue Mountain Lake, that her stomach difficulties have increased, and thinks her neck has enlarged. September 18: Goitre very much diminished.

January, 1900: Practically well.

CASE XXI.—Mrs. R. A. P. Æt. about 56. From Atchison, Kansas.

June 11, 1898: Pulse 140. Her symptoms were of more than two years' standing, before the goitre developed two years ago (4 years). Symptoms consisted of attacks of palpitation, with much disturbance of the stomach, with attacks of vomiting, followed by great prostration. Has become much emaciated, and lost so much in strength that she could scarcely walk; thinner after two years of these symptoms. Great tremor of the hands. Goitre developed, with exophthalmos. Present condition extremely weak; great weakness of the voice; very much troubled with gastric flatulence and nausea. July 22: Went to Gloucester, Mass. Writes that she has gained slightly in weight. Pulse 96 after taking blue pill, but runs up to 120 afterward. August 10: Much troubled with diarrhœa and increased weakness. August 20: On the 18th, had an attack of faintness, which she at once relieved by a blue pill. Very nervous at times. Has some swelling of the feet. September 6: Writes she is feeling better. September 16: Returned to New York. I find that she has lost ground. Weather had been very damp and depressing. She has grown thinner; has much insomnia; diarrhœa continues; tremor very marked. Pulse 106, and irregular. September 29: On the 22d had a severe diarrhœa from eating clams. On the 28th took a little clam broth, had more diarrhœa. To-day pulse irregular, with pauses. September 30: Left for home. December 20: Writes that she is greatly improved; has gained 5 pounds; less depressed.

January 25, 1900: Writes that she has improved very markedly, except that tachycardia continues. Bowels much better, but move twice a day; hands a great deal better for writing.

October: Reports steady improvement.

CASE XXII.—Miss M. R. Æt. about 44. Dressmaker, from Glens Falls, N. Y.

March 8, 1899: Comes for migraine, which she has had throughout life, but lately worse. Becomes very sick and prostrated lately with attacks, accompanied with pain down the left side of her neck, but not in the ear. Pulse 118. No exophthalmos; but right lobe of the thyroid somewhat enlarged. Says it

often makes her collar too tight. No palpitation; no tremor. Very slight tremor in the lids on closing. October 9: Called with the story that instead of having headaches every week they have now become quite infrequent. Pulse now down to 84. Swelling of the right thyroid diminished; but complains of a great deal of pain in the left side of the neck and down the left arm. Says that before she came to me she would have these arm pains severe enough to make her faint, though much lighter in the right arm and in the legs.

April 8, 1902: Now comes for a sense of gastric trouble, affecting breathing. Pulse 120. Frequent headaches again. Some loss of hair; pain in the left neck; left ear sensitive to touch. No tinnitus. Much troubled with black specks before her eyes, when she has headache. No tremor anywhere; no weakness of knees; no itching. Bowels regular; but some irritability of the bladder. Goitre disappeared; but lately slight enlargement again of the right lobe. Always worse mornings.

CASE XXIII.—Miss F. C. Æt. 22. Sent by Dr. H. M. Kinghorn, of Saranac.

April 3, 1899: When nine years old this patient had goitre and pronounced exophthalmos, which goitre continued (fluctuating in size) until last summer, when it disappeared. She states that this was positively so last October. She then went to Saranac, and about two weeks afterward goitre developed. Dr. Kinghorn then saw her, and she had von Græf's symptom; but this has now disappeared. Patient has always been very nervous; much troubled with migrainous headaches and frequent nausea. When she went to Saranac, she vomited very often after meals. Three years ago lost her hair freely, but it has grown again. Has had pains in the left ear, but no other pains. Pulse 120. This patient's temper very variable and obstinate.

(Mrs. C., her sister, aged 32, when 14 years old had pronounced goitre. This has subsided. Their mother also has a goitre of many years' standing, beginning when she was a young girl. Her mother, all four sisters and her brother, are all martyrs to sick headaches.)

April 3, 1900: Last report, patient much better in her stomach and in her headaches; but very difficult to persuade to take the remedies.

CASE XXIV.—Mrs. W. E. W. Æt. about 38.

June 20, 1899: About January she had the grip. Since then has had a great deal of gastric distress and disturbance after eating, with palpitation, and occasional painless diarrhœa.

Tremor of the hands, especially the right, so that she cannot write except evenings. Has sharp pains in the ears, especially the right ear. Pains in the shoulders, left arm and legs. Great weakness of the knees. Has lately noticed the falling of her hair. Found moderate enlargement of the thyroid, equally on both sides; no exophthalmos, but tremor of the eyelids when closing. No pains in tips of fingers or toes. Her mother (who died when the patient was ten) had goitre and frequent sick headaches. Has a sister with goitre. Has lately lost flesh, from 120 pounds to 106 pounds. Always feels markedly worse in the mornings, with increased nervousness then. Moderate Stellwag's. Has frequent attacks of pains in the eyes; also has attacks of hunger. June 27: Not much changed, except less flatulence and dyspepsia. Diarrhœa persists. Pulse 120 to 130. July 12: Digestive symptoms much better; pains better; less pain in the ears. Says symptoms of great sensitiveness at the external rim; palpitation continues. Morning wretchedness very pronounced. Pulse 116. Weight the same, only 106 pounds. July 21: Diarrhœa six to eight times a day. Same ear pains. Pulse 124. Still has pain in the eyes. July 31: Better. No more diarrhœa. Pulse 110. August 14: Not so good a report. Much pain in the ears. Soreness about the stomach, and rheumatoid symptoms in her limbs. August 28: Better; but still has pains in the ears. Pulse 110. Troubled now with insomnia. September 18: On the whole, better. Rheumatoid pains better; dyspeptic symptoms less; but bowels move too freely. Pain in the rim of ears still. Insomnia still; knees sometimes weak. September 28: Pains in ears very sharp. Pulse 104. October 17. Not so good a report. Insomnia and more neuralgias. Diarrhœa better, but she still has three loose movements a day. Pulse 106. October 24: No improvement. Diarrhœa continues. A good deal of palpitation.

February 5, 1900: Comes with the report that she has been so well, did not think it necessary to come. But lately from excitement had a relapse of palpitation. Has gained in weight; eyes look more natural. Pulse 112. February 15: Complains of itching. March 22: Pulse 82, but feels weak. Her pains gone. June 8: Has been doing very well. Goitre gone; exophthalmos gone. July 2: Been doing very well. But has occasional palpitation; some itching; some falling of the hair. December 1: About well. Occasional pains in the ears. Some spots of discoloration in the skin.

May 11, 1901: Comes virtually free of Graves' Disease, except that lately has had some pain in the ears and some palpitation. Pulse 86.

CASE XXV.—Miss O. B. Æt. about 35.

July 11, 1898: Has been a chronic gastric dyspeptic, for which she has been treated by a number of physicians. Is very much emaciated. Last April first noticed that she had pronounced tachycardia. For a good while before had itching of the skin; and lately perspirations. Not much headache. But she has pains in the ears, especially in the left, with a sense of throbbing; also pains in the fingers; but otherwise no neuralgias. Sleep now fair; but has weakness with palpitation. Tremor very general, causing much annoyance in her writing. Feels especially weak in the knees. No vesical irritability; bowels natural. July 18: On the whole, a favorable report. Is troubled with a sense of hunger.

March 24, 1899: Exophthalmos increased. Says she is a great deal better in most respects. Tachycardia continues. Pulse 130. Has pain in the left ear, the rim of which was extremely tender. June 14: On the whole, better. No goitre now; nor marked exophthalmos, but marked Stellwag. This patient never had migraine, but suffers now from pain in the eyes on going to bed and on waking. Always wakes in the morning with a start and palpitation. No rheumatoid pains. Dreads going on the cars on account of feeling weakness in the knees. No stomach troubles, but she has attacks of sudden diarrhœa without any apparent cause. July 14: Feeling much better. Pulse still 120 to 130; not intermittent. Slight right goitre. December 15: Comes with a story of having been much improved till lately; occasional attacks of diarrhœa; occasional pain in the left ear still. Pain in the eyes frequent; exophthalmos moderate, but Stellwag pronounced. Goitre disappeared. Pulse 104. Has gained in weight.

January 12, 1900: Relapse. Vomiting and diarrhœa. When diarrhœa occurs her face turns crimson. Pulse 118 July 13: Comes with the story of general improvement. Gained in flesh and strength. Still characteristic pains in the eye, especially the left; also rheumatism in the right knee, and some in the tips of the fingers. Chief trouble now is nervousness, itching, and especially pains in the eyes mostly on trying to open them after sleeping. Stomach troubles her now. Bowels occasionally loose. Slight Stellwag and slight exophthalmos. Tremor in the lids much less; goitre again but very much less. No migraine in herself or family. Pulse 110.

June 18, 1901: Pulse still 130. Has headaches with blurred vision. Pains in the right iliac region over the appendix.

September 5, 1902: Has gained a great deal in weight. Goitre quite small. Stellwag pronounced. Much falling of the hair,

also of the eyebrows. October 13: Quite a relapse. Pulse 130. Very nervous. Has bulimia and headaches. Much troubled with a short cough; no expectoration. Some difficulty in passing water.

CASE XXVI.—Mrs. M. F. Æt. about 41. Of Poughkeepsie. The mother of three children. Brought by her physician, Dr. L. C. Wood.

December 1, 1899: First noticed an enlargement of the thyroid seventeen years ago, a year after her marriage; but at that time was not aware of having any tachycardia. Was first aware of this symptom by an attack of long illness, ushered in by quinsy. She has had repeated attacks of quinsy since. The feature of her case is that the goitre is but moderate, slightly more on the left side, but has remained constant for years. She has had rapid action of the heart for several years; but otherwise has enjoyed very fair health. She denies having any trouble with her stomach. Sleeps very well; no headaches; no neuralgic symptoms whatever. But for the palpitation, would consider herself quite well. She has simply a slight tremor in the right hand, but none in the rest of the body. No weakness of the knees; has no rheumatism. No family history of migraine.

On examination pulse peculiar; two quick beats, then a third fuller, then an intermission; then a rapid vibration rather than a pulse. Then the same cycle over again. On auscultation the sounds are uniform, but almost too rapid to count; both sounds at the base alike; at the apex, the first sound more blowing. No murmur. Strong pulsation in the arteries of the neck and of the thyroid. No exophthalmos whatever; but lids tremulous on closing. Patient cheerful and equable; and has no nervous complaints of any kind.

This case of itself would negative gastro-intestinal origin. Doubtful if the tachycardia is not due solely to pressure of the tumor in the neck.

CASE XXVII.—Miss A. T. Æt. about 50, but looking older. Sent by Dr. G. B. Philhower, of Nutley, N. J.

November 20, 1899: Has a pronounced goitre for 35 years. Has an aunt who had one, but which disappeared; also a female cousin who had it a year; both on her mother's side. Her mother's whole family are migrainous, but not her father's. This patient had migraine for years, but has none now. Her present tachycardia she dates only six weeks. But since having the grip a year ago, her health has been failing; and all through

this past summer she had frequent attacks of nausea. These culminated in tachycardia, with still occasional nausea; much nervousness; and tinnitus, without loss of hearing, very annoying in the left ear. Has had this tinnitus over a year. Lately she has a tenderness on touch of the right auricle. It is red in the upper part. Feeling very nervous, with a sense of inward tremor. Eyelids tremulous. Pronounced tremor of the tongue, but not of the right hand. Pulse is very difficult to count, being not only rapid, but a few beats very thready. No neuralgias. Bowels constipated, but occasional diarrhœa. Some vesical irritability. Lips too red; tongue very clean and inclined to redness. Does not feel worse in the mornings. Very insomnic. Chief trouble is the tachycardia.

July 19, 1900: Was better. For a while did have rheumatoid symptoms, but not now. Insomnia improved, but heart action still very thready. No pains in the eyes; no headaches. Has been better of her nausea; but it sometimes comes on temporarily. Much troubled with inability to take milk.

1901: Heard through the doctor that she had very much improved.

CASE XXVIII.—Miss J. W. Æt. 23. Brought by Dr. Herman Jarecky.

January 3, 1900: Her family say she had had a large neck for some years. Now the goitre is quite pronounced; right lobe most. Moderate exophthalmos. Pulse 120. Chief symptoms: tachycardia, general tremor, perspirations and itching; lately moderate diarrhœa. Previous history of marked constipation. Frequent pains in the bowels not connected with diarrhœa. Has frequent headaches of migrainous character. One sister (deceased) had headaches. No ear symptoms; no pains, except moderate in right shoulder. Has weakness of the knees. Has had some epistaxis. No loss of hair.

CASE XXIX.—Mrs. M. L. B. Æt. 42.

April 10, 1900: Has noticed increased indigestion, with a great deal of flatulence in her stomach, with occasional palpitation. I was at first misled, however, by not finding tachycardia. Yet she has had attacks of causeless diarrhœa; weakness of the knees; inward tremor; neuralgias in the back of the shoulder and up the neck, affecting the right ear; some shaking of the right arm; tremor of the lid; and now enlargement of the right thyroid.

This is a case, therefore, of Graves' Disease without tachy-

cardia. She has been losing flesh. Her mother had double goitre, without exophthalmos.

April 25: Claims that gastric flatulence is no better. Tremor increased in her right hand. Bowels loose; also has attacks of palpitation. But pulse only 86. May 10: On the whole, better. Bowels not loose, but the gastric symptoms of flatulence the same. Pulse still only 80. But she says she has palpitation at night, and cannot lie on the left side. May 23: Considerable improvement. Goitre diminishing, and other symptoms better; but gastric flatulence continues. June 5: Flatulence much improved; but for two days has had a return of diarrhœa; pain in her left ear, and general nervousness. Pulse 90. As usual, worse in the mornings. June 19: Has been better, but some looseness still. July 9: Improving; but with occasional looseness of the bowels. August 6: Relapse. Good deal of diarrhœa; also morning nausea; feeling quite shaky. Has had some pains in throat. No pains in left ear now. October 16: She has been doing very well, until she had a great fright, since which all the symptoms have recurred, including pains in the ear. This fright caused tachycardia for the first time. But this subsided. October 30: Better All symptoms better, except flatulence, which occurs after each meal and in the night. Pulse 82. December 14: Has been doing well, except once three weeks ago, she had an attack of diarrhœa and vomiting. No ear pains. Goitre diminishing.

November 8, 1902: Heard that for the past year she has been entirely well, and that the goitre had disappeared.

December 27: Heard from her sister that this patient is now quite well. Goitre has disappeared, so that she can now sing in public with a low necked dress on.

CASE XXX.—Mrs. M. Æt. about 35. Married seven years; has two children. Consultation with Dr. J. Lyon.

February, 1900: According to her statement and the doctor's, she had her symptoms first about seven weeks ago. At my visit, she was very prostrated—in bed. Pulse 160. Unable to rise from her bed on account of weakness. Suffering from severe headaches and active diarrhœa. October 4: She now comes to my office, saying that she is very much better. Goitre diminished. No exophthalmos, but eyelids very tremulous. Pulse 112. Has pains that are very distinct in the tips of her fingers, but nowhere else. Since her attack in February, she has had ptosis of the left lid. Says, that she is no worse mornings. Says, the very first symptoms she had were steady headaches. Reports, that sister and father are very migrainous.

CASE XXXI.—Mrs. A. W. Æt. about 42.

March 5, 1901: She has had goitre for three years. Has been a chronic dyspeptic. Frequent attacks of tachycardia. Quite emaciated. Exophtalmos. Pulse 140. Manner very much agitated. Complains of neuralgias in different parts of the body—pains in the fingers, in her heels and in her toes. Her family state, that she has always been of a very peculiar disposition, very erratic, and inclined to religious extravagances. She is often found on her knees, and spends the most part of the night praying. She now refuses to come to me for any medicine, because the taking of any medicince would imply lack of faith in God. All she will agree to is that she will submit to rules of diet. She has great weakness of the knees, and has had many falls. Refuses to have any attendant in the street, because that would imply lack of faith. Has frequent headaches and occasional bronchitic cough.

I saw this patient a number of times, until November, 1901, but as she refused all treatment her symptoms continued to increase, until she became a confirmed paranoic. She always denied being any worse, lest that might imply lack of faith.

CASE XXXII.—Miss J. G. Æt. 50. Summit, N. J.

May 14, 1901. Comes for a large goitre, which began in childhood; did not begin to enlarge seriously until she was five years of age. She is, therefore, a case where Graves' Disease was engrafted on parenchymatous goitre. Meantime, has had excellent digestion; no trouble with the bowels; never had migraine; nor any of her family on either side. She does not admit any of the associated symptoms of Graves' until last October, when she had a severe illness of some weeks' duration, till the middle of January, when she began to sit up and slightly convalesced. During this attack, her temperature rose between 103 and 104. While convalescing, she had a series of Graves' symptoms. Pain in the head, especially occiput; stiffness of the neck, especially of the left side muscles; great pain in the left shoulder and arm, but nowhere else. Some vertigo on first attempting to walk; great itching of the skin; some irritability of the bladder. Such shaking of the right arm that she could not feed herself. Always felt much worse in the mornings. Latterly has had acute pains in the stomach, not connected with taking food. No falling of the hair; but says that it turned gray during her illness and on recovery regained its color. While she was sick her voice became very harsh. Goitre extends on left side down to the clavicle, and upon the sterno-cleido muscle; is tight

across the isthmus, causing inspiratory stridor. Has some dyspepsia, with occasional choking. No symptoms of Graves' now, except pulse 100, and considerable tremor of the eyelids. July 8: Returned, stating that she took capsules only two days, when she had an attack of grip; then left them off to take her physician's treatment. Pulse 108. July 24: Writes under date of the 16th, cannot take capsules, make her nauseated. Has pains in head, neck and shoulders, and general weakness all over the body.

I recently saw the notice of the death of this patient, but have no particulars.

CASE XXXIII.—Mrs. P. Æt. 49. Wife of Dr. P., of Stamfordsville, N. Y.

November 23, 1901: Has been a chronic gastric dyspeptic for years. About three years ago had serious domestic trouble with her son. Began with attacks of palpitation then, but dates her present illness about a year when she noticed enlargement of the thyroid, mainly the left lobe. About six months after, great aggravation of dyspetic trouble, with great flatulence; tachycardia, with very weak and irregular pulse, the beat at the radial only about 81, the heart beats 140. Extreme nervousness. Tremor in the hands not pronounced; scarcely any lid tremor; general weakness, especially of the knees, so that she once had a bad fall. No pains, except in the left knee. Great insomnia. Much troubled with sense of heat. Always much worse in the mornings. No itching, no vesical irritability; some constipation; some loss of hair.

I learned of Mrs. P.'s death ten months after.

CASE XXXIV.—Mrs. E. G. W. Æt. 54.

September 26, 1910: One sister (about 35) had goitre. Father and brother died of rheumatism, an older sister (about 60) had rheumatism late in life, and is now crippled by it. Mrs. W. has been dyspeptic and troubled with her stomach for years. She began to run down in health and lost flesh for a year past, weighs now only 81 pounds. About December 1, 1900, had a severe illness, pronounced gastritis, which confined her to bed for five weeks, and along with it she had bronchitis. With this she had attacks of palpitation, but admits that she had often been subject to palpitation before. Had long been nervous, but now the nervousness became constant, with a sense of inward tremor and general weakness; tremor much more in the right hand; weakness in the knees so that she has had several falls. Then came on a distracted throbbing in the ears, of which she complains greatly, particularly the left ear, with some pain in that ear.

No deafness; no eye symptoms; no exophthalmos, tremor of the lids moderate, more in the right, always worse in the mornings, and depressed to weeping then. Better afterwards. More palpitation after eating. The only pain admitted of is a rheumatoid affection of the right shoulder and arm, with stiffness of the right fingers. Flatulence in the stomach; no diarrhœa; inclined to constipation; occasional pronounced weakness of the voice. Greatly troubled with insomnia, has lost a great deal of hair. Pulse 108, rather high tension, and sometimes irregular. Heart sounds sharp at apex, but no murmur. Her goitre, which is more on the right side, first noticed about December 1, 1900. On first waking in the morning the eyelids and teeth shake. Patient very much emaciated. Has constant cough, with general mucous râles. September 30: Much troubled with her cough and the roaring in her head. Now has pain in her left arm. Feels less nervous. Pulse has been down to 82. Sleep bad. Bowels loose. October 2: Much palpitation. October 9: Great complaint of insomnia. October 20: Improving in all respects, but still complains much of the left ear trouble. October 23: Pulse 110. Complains of palpitation, tinnitus and insomnia. October 28: Has ganed 5½ pounds since last weighed; altogether 7 pounds. But still insomnic. November 2: Complains of more palpitation. Tinnitus better. Pulse stronger. November 7: Improving in every way. Stronger, but palpitation still. November 11: Gained 6½ pounds more in two weeks. Feels much improved. Tinnitus better. Pulse 100, full and forcible, and increased after eating. November 16: Not so well, from increased palpitation. November 21: Marked improvement. Pulse down to 82, and softer. November 25: Continued improvement. Better sleep. November 30: Continued improvement. December 7: Some strain from illness of her husband, with increased indigestion and flatulence. December 12: Doing well. Weight increased 4 pounds in two weeks. Still complains of tinnitus. December 16: Improved in every respect, excepting the tinnitus, of which she complains very much at night especially. December 31: Tinnitus much worse again. Weight now 114 pounds.

January 9, 1902: Quite depressed, with relapse from a cold, with severe bronchitis and bloody expectoration. Temperature 99. January 15: Temperature normal. Hemoptysis ceased. Still has short cough. January 20: Influenza in the head, and cough persists. Expectoration bloody again. Feels nervous and depressed. January 22: Much improved; no râles, but dry sibilus. Pulse only 84. Since resuming the old medicines (for Graves') her heart has quieted down (Mr. W. says) to 74.

January 29: Another attack of bronchitis. February 1: Pulse only 78. February 3: Better. Feels stronger, but still insomnic. February 13: Doing well in most respects, but complains greatly of nocturnal attacks of indigestion, with internal distress and irregular pulse. March 8: Went South February 15. Writes (from Palm Beach), has no indigestion; but throbbing in the head and the tinnitus continue. March 21: Returned from Florida. Enjoyed the trip. Sleep good. Tinnitus less. Pulse 96. March 27: Comes for attacks of flatulence. April 1: Excessive gastric flatulence. Pulse 102. Insomnia, palpitation and mental depression. Constant borborygmi as she sits here in the office. April 5: Curious that she has good days, but on going to bed palpitation comes on with excessive flatulence. April 25: Comes improved in every way. May 5: Gaining strength, weight and color. Still complains of tinnitus. May 13: No gastric flatulence, but borborygmi. May 29: Has been doing very well. Tinnitus diminishing. Pulse 88. November 22: Comes almost transformed. Total increase in weight from a year ago from 81 pounds to 142 pounds. Complains still, however, of the tinnitus. Goitre very much diminished, only one-quarter the former size.

May, 1903: Patient's goitre has disappeared, and the only one of her former symptoms left is a slight tinnitus.

CASE XXXV.—Mrs. G. D. T. Æt. 35. An Armenian. Consultation case.

February 6, 1902: Goitre for five years; very slight exophthalmos. Goitre increased in size, so as to interfere with breathing. Pulse very weak, 100. General weakness; weakness of the knees, pronounced tremor of the lids, moderate of the hands; insomnia; has lost some hair; has a great many headaches; bowels constipated.

CASE XXXVI.—Miss G. A. S. Æt. 22. Sent by Dr. Dawbarn.

June 6, 1902: First noticed goitre between seven and eight years ago. This increased so that the doctor had to operate to relieve the dyspnœa. No migraine in herself or her family. But a story of rheumatism on the father's side. Patient has had no digestive troubles whatever, until of late she has a good deal of flatulence. No diarrhœa, but constipation. No exophthalmos, but eyelids widened; and tremor on closing eyelids. No rheumatoid pains anywhere. Nothing about the eyes. Much tremor of the arms. Weakness of the knees, so that she feels as if she would fall. Nervousness moderate; no itching; no

irritability of the bladder; lost a great deal of hair; feels very tired in the mornings. Goitre used to vary in size, but grew to 17 inches in circumference. After operation on the left and medium line, it is now down to 13 inches. Pulse 130. Heard from the doctor that she was getting better.

CASE XXXVII.—Mrs. K. Æt. 42. A fleshy woman. Sent by Dr. F. P. Hammond.

October 20, 1902: Has lately been growing very obese. Has long been troubled with gastro-intestinal derangements, latterly obstinate diarrhœa. Pulse 116. Slight tremor of the eyes. Pain in both ears, but most in left. Pains in tips of fingers, and in tips of toes, latter very troublesome. No pain in heels. Complains of many neuralgias everywhere. Frequent headaches; weakness of the knees so that she dreads falling. Chief complaint pain in the region of the heart, with tenderness to touch from the third to the sixth rib on left side. No heart murmur. Extremely nervous and tremulous. Hair falling out. Occasional itching. Frequent vesical irritability. Her mother has to go to bed for a day with severe migraine.

CASE XXXVIII.—Mrs. E. D. Æt. 32. Of St. Louis, Mo.

October 4, 1902. Has been troubled with diarrhœa for a great many years. Had goitre for four years; and for some years before the goitre became extremely dyspeptic, with chronic flatulence, both gastric and intestinal. Went to Paris to be treated for it, but without avail, if not made worse, by anti-dyspeptic remedies. Was extremely nervous. Went to Dr. Weir Mitchell for her nervous symptoms. He put her on the rest cure, when she got decidedly worse. But she says the goitre improved with his application of galvanism. The symptoms in her case are: Tremor of the eyelids; difficulty in using the right hand in writing; weakness of the knees, and once abasia. But muscular tremors not as bad now as formerly. Has lost hair considerably; has itching and vesical irritability, especially at night. Very insomnic. Pulse 106. Occasionally wakings with palpitation at night. Negative symptoms: No general pains; no rheumatic pains. To-day for the first time had pains in her ears. No headaches; but her mother is a martyr to migraine and her own little daughter. Slightly worse in the mornings. Goitre is more on the right lobe, but extends down well to the clavicle. Her mother and aunt had goitre, but says that her mother and aunt were cured by local applications of iodine and sitting in the sun.

July, 1903: Her husband writes that following my treatment she has greatly improved and the goitre is rapidly lessening.

January 10, 1904: Report of continued improvement. Bowels now regular. Pulse 88.

CASE XXXIX.—Mr. H. S. Iron manufacturer. Æt. 35. Resident of St. Louis.

January 26, 1903: Strong and vigorous-looking man. He always enjoyed good health, except a severe gastric trouble when he was a boy. Has been a fast eater; of temperate habits. He began last August to be extremely nervous, with much insomnia. He had then some mental strain. This nervousness became associated with general tremors, especially of his legs; and his handwriting became so affected, as to trouble him when signing checks. Lately he has been having attacks of diarrhœa, with much abdominal distress; frequent nausea; with great weakness of the knees. In November he had a sudden fall. He has rheumatoid pains in one joint after another; some loss of hair; some irritability of the bladder; excessive itching. No sweating; but marked bulima. Does not feel worse in the mornings. Eyelids do not tremble. No headaches, nor story of migraine in his family. Slight exophthalmos. Moderate enlargement of the right thyroid lobe. Pulse 100.

CASE XL.—Mrs. S. Wife of a physician. Æt. 31. Of Newport, R. I.

January 21, 1903: A native of Vienna, Austria. She was suddenly attacked in December, 1897, with severe diarrhœa; sometimes with vomiting. This confined her to her bed for three months. While she was getting well, she was found to have very violent heart action. She became extremely prostrated. Exophthalmos and goitre were first noticed in February, 1898. No family history of migraine, but the patient used to have headaches. She has but little stomach distress, but a great deal of gastric and bowel flatus, with repeated attacks of diarrhœa. She now has frequent headaches, with scotoma. No pains anywhere, and no ear symptoms. Some tremor of the hands, affecting the writing; but no sense of general tremor. Great weakness of the knees; loss of hair was the first symptom of all; some itching; some vesical irritability; and has pronounced bulimia. Feels worse in the mornings. Pulse 100. Goitre moderate, and has been very variable in size. Pronounced exophthalmos of the left eye. Right eyelid droops. Extremely nervous.

April 4, 1903: Was much improved for a while; but a month

ago was suddenly taken one day with a rush of blood to the face and head and ever since her symptoms have been worse.

November 30: Has been much better but the exophthalmos in the left eye is the same. Occasionally has headaches, with transient aphasia. Her bowels still inclined to be loose. Pulse 92.

January 5, 1904: Pulse now normal. Much less headache; and less flatus.

CASE XLI.—Mrs. H. H. P. Æt. 32. Patient of Dr. L. W. Vroom, Ridgewood, N. J.

January 12, 1903: This patient claims she was quite well until two months ago; but that she has been dyspeptic for years; has also been greatly subject to headaches, but no rheumatism. Her first symptoms were, that she began to be very nervous, and had pains at the root of the neck, when she discovered that her thyroid was enlarging. This enlargement varies from week to week, the right lobe the most. She has a great many headaches now, more on waking; but she has a fever in the afternoons. No eye symptoms, except tremor of the lids on closing. No ear symptoms, only pain in the fingers. Hair has been falling out for a good while. Her chief symptoms are: Great general weakness; weakness of the voice, so that at times she can scarcely be audible; constant general tremors, but not in the tongue; right hand so affected that she cannot write. She has been losing flesh; has a great deal of sweating; moderate flatulence of the stomach; bowels constipated. No family history of migraine. Pulse from 130 to 140 and weak.

June 26: Bad report. Temperature rises every afternoon from 102 to 103. So weak that she cannot leave her bed. Breath very offensive. Has great pain in the thyroid.

July 1: Report of rapid improvement under the treatment advised. Pulse has been down to 88; voice returning; temperature down to normal mornings, afternoon 100. Pain in the goitre gone. Less nervous; breath better. Tongue much tumified, and raw on the edges.

July 15: Steady improvement continues.

September 1: Has greatly improved; goitre almost imperceptible. No fever, pulse 102. Some tinnitus. Tongue now clean, but large and edges indented. Flatulent still, but much better; bowels still constipated; much insomnia; occipital headaches in the mornings; sweating much less.

December 29: Comes improved in every way. Has gained markedly in flesh. Goitre gone, all she feels now is a throbbing in the neck. Pulse 90.

CLINICAL HISTORIES OF CASES WITHOUT GOITRE.

CASE. I.—Miss L. W. Æt. 35.

Tachycardia for nine years. General inward tremor, and tremor of the tongue and hands. Weakness of the knees. No nervousness. Never had headaches till this illness began, when severe migrainous attacks became frequent, with attacks of blindness. Constant tendency to gastric disturbance. Occasional causeless diarrhœa. Frequent rheumatoid pains in various parts. Marked tenderness of the left ear. Tinnitus. Occasional vertigo. Frequent sweating. Paræsthesiæ in the throat, fingers and limbs. Vesical irritability. Loss of hair. Itching. Frequent attacks of spasmodic cough.

This case is of interest for prolonged symptoms without goitre, parallel to her sister's case, who had similar symptoms for three years and then developed goitre.

November 2, 1893: Miss W. has a peculiarly equable temperament, without a trace of hysteria. She complains of nausea, and a constant tired feeling, with pains in the left wrist and under the left shoulder blade, and sometimes in the right shoulder.

May 3, 1894: Is troubled with excessive sweating, without any known cause.

April 20, 1895: Complains of pains and aching under her right scapula. Very tired in the evenings. Sudden pain in her left ear and left arm. June 21: Comes with a story of chills every night, and increased pain under her right shoulder.

March 10, 1896: Quite affected by the illness of her brother. Has turns like malaria, and tremor of the tongue. April 6: Has attacks of pain in the left side of her head, with tenderness over the left ear. Has never been subject to headaches. Feels prostrated in the afternoon, and sweats at night. April 18: Rheumatic symptoms in hands and fingers; severe backache, and in shoulders. May 27: Less pains, but pulse 120. May 30: Feeling of general weakness. Some aching in her throat. Pulse 118. December 7: Better in her neuralgic symptoms; but now troubled with frequent headaches. Pulse 116. Troubled with bronchitic cough for five weeks.

April 12, 1897: Pulse 120. Sense of inward tremor throughout the whole body while sitting still. Sense of weakness in knees. Darting pains, with throbbing, in the left ear. June 25: Symptoms more pronounced; has migrainous headaches; sense of tightness in the throat; sweating; sensitiveness to touch of the left ear; occasional severe pain in the right hypochondrium. Pulse 114. July 6: Has attacks of blindness, first in one eye, then in the other; and sometimes in both eyes.

March 8, 1898: Throughout the last summer has felt a variety of the symptoms described; but has been much better of them this winter. Find her pulse, however, 110, with high tension. She finds that her diet is all important. May 14: Had an attack like gout in the right toe; also sudden pain in the right knee. Comes to-day with some of her old symptoms; constriction in the throat; occasional pains in the ears; also pain in the shoulder; occasional palpitation in the morning. Sometimes has dizziness. Pulse 108. June 16: General rheumatoid pains, especially in the feet, when walking or standing. Some headache; occasional palpitation, and pain in the ears. July 16: Great tenderness of the left ear. Pain in the right little finger; also in her heels. Has a feeling of being sick all over. Pulse 96. Had causeless diarrhœa one night. November 7: Relapse of her old symptoms. Pain frequent in the cardiac region, radiating to the left arm. Tenderness and pain in the left ear, very frequent, radiating to the muscles of the left neck; sometimes in the right ear; also spasmodic cough. Pulse 122. Sleep rather disturbed. Has some flatulence in the stomach; pain in the eyes, without former blindness. November 29: Feeling better. Sleep good. Pulse 108. Attacks of constriction of the throat. Spasmodic cough; pain in her heels.

April 29, 1899: Pains in the fingers, hands, toes and top of the foot; occasional nausea. September 22: Has passed a good summer, lying in the hammock, and taking it quietly.

January 22, 1900: Old left ear sensitiveness has returned; occasional attacks of blindness in the right eye. Pulse 104, but high tension. November 8: Has had a good many of her old symptoms; much affected by her sister's death. Sometimes temporary blindness of the left eye. Now has numbness of the left thumb and hand. Pulse 116. Frequent but slight itching. Sometimes irritability of the bladder; considerable loss of hair; bowels constipated.

January 28, 1901: Has had headaches for a week. Pain in both eyes; attacks of blindness in the right eye; attacks of palpitation, with pain in the region of the heart, radiating into the left arm. Headache with nausea. Pains in the tips of fingers

of left hand. Pulse 92. February 13: Still some headache, but not so severe. Her head for some time has felt uncomfortable. Yesterday had some vertigo. Very rheumatic in her knees and left elbow. Pulse 86. February 15: A good deal better of the rheumatism; other symptoms better, except blindness in the left eye. Pulse 106. February 22: Better in every respect, except rheumatism in hands, wrists and knees. March 21: Some blind attacks in the right eye; some flatulence, particularly evenings; occasional insomnia. Has trouble in the morning to hold up her head; otherwise does not feel worse in the mornings. Pain in the left neck. She now says that at the beginning, four years ago, she had tremor of the hands and weakness of the knees.

April 22, 1902: Has been very well all winter. Still has attacks of her old blindness in the right eye. Pulse 104. May 7: Complains again of a sense of constriction in her throat. June 20: Pulse 110. Feeling in throat returned. October: General improvement, but pulse still 100.

REMARKS.—This history is condensed from extensive notes during the long time when she has been under my constant observation. The persistence of her tachycardia is noteworthy, her pulse never below 100 for nine years, after which it fell to normal on her full recovery. A prominent feature has been her pains, which partook more of a gouty than of a rheumatic character, and yet developed in the peculiar localities of pain in Graves' Disease; and while remedies for gout failed to relieve them, a mercurial laxative always proved the best remedy. Whenever she violated instructions, by partaking of red meats, all her various symptoms were soon aggravated, particularly the tachycardia, and the head and eye symptoms.

CASE II.—Mrs. L. Widow. Æt. 50.

Prolonged severe diarrhœa, with great emaciation, proceeded by tachycardia for two years. Marked general tremor, and of the hands. Great prostration. Constant headaches. Insomnia. Much gastric distress. Severe rheumatoid pains. Vesical irritability.

October 1, 1891: First seen in consultation with Dr. Emil Mayer. She had been for a year troubled with obstinate diarrhœa, always worse in the mornings. Along with this diarrhœa, she had become greatly emaciated; had continued tachycardia for two years previously. Found pulse 150. Frequent

rheumatoid pains in different parts of the body. Greatly troubled with gastric flatulence; very insomnic; constant headaches. With these symptoms she complained of excessive nervousness, and weakness of the voice. I found her very weak and prostrated, unable to leave her bed; with great tremor of the hands; also much troubled with vesical irritability. I diagnosed Graves' Disease, and recommended full treatment. She responded very promptly to the treatment, gained rapidly in flesh and strength; and in three months felt herself quite recovered.

October 25, 1893: After considering herself perfectly recovered in the interval since the last date, she now comes for much vesical irritability. November 6: Vesical irritability better, especially at night, but persists during the day. November 30: Becoming insomnic again, and feeling a relapse of her old symptoms.

October 2, 1894: Been on the whole better; no tachycardia. But complains of soreness in the knees, with twitching of the muscles, with paræsthesiæ in the arms, and numbness and coldness in the legs. Her old symptoms much better.

June 3, 1895: Been on the whole very comfortable since last date; but comes to-day with much the same symptoms of pain in limbs, like sciatica, also a good deal troubled with nervousness and some swelling of the knees. Troubled now with blepharthero spasm. Pulse quite normal.

October 25, 1898: This patient has remained entirely free from any of her old symptoms.

REMARKS.—This patient had been treated for nearly three years by more than one physician with various symptomatic remedies which wholly failed to relieve any one of the symptoms for which they were prescribed. Because she had neither goitre, nor exophthalmos, her physicians never thought of Graves' Disease; but as she progressively grew worse, till she became too weak to sit up in bed, a serious prognosis was given. It was very noteworthy how soon she improved after she was treated for Graves' Disease.

CASE III.—Mr. A. B. S. Æt. 42. Lawyer, light complexion. *Prolonged gastro-intestinal trouble, with a definite beginning. Always worse in the morning. Persistent tachycardia for five years. Nervousness as of fear. Weakness of the extremities, with paræsthesiæ. Depression and mental clouding in the morning, proportioned to his diarrhœa. Recovery.*

October 25, 1895. Fairly well nourished. He says: A year ago last May, having before that had no gastric or other trouble with his stomach, he was suddenly taken with nausea and distress of the stomach; and that this has continued ever since. He only had occasional relief while on outings.

His symptoms are: Nausea, and an ill-defined sense of distress referring to the stomach, without any aching or heavy pain, not radiating anywhere, and not aggravated by eating. Most pronounced on waking in the morning; not worse when stomach is empty, and not relieved by eating. Can lie on the left side as well as on the right. Pulse regular.

Examination: Knee jerks normal; no ataxia; no shooting pains; found no evidence whatever of gastritis; has frequently had his stomach washed out, without anything but clear water coming up. Examined him for movable kidneys, but could make nothing out. Says that he always has on a movement of the bowels a feeling as if he had diarrhœa, and this feeling lasts sometimes, though he has no looseness. Found pulse 130. No heart murmur. Says the eructations from his stomach are offensive to him, but with no taste of food. Claims that diet does not make any difference.

November 4: Feeling better; morning distress better. November 19: Quite a favorable report, though with occasional relapses. November 30: Relapse of all his old symptoms; has sensations referring to his stomach as of old, without pain, but nauseated and with diffused discomfort. Pulse 120. Had slight diarrhœa one day. His chief symptoms are, when these gastric disturbances set in, he has a sense of weakness and aching coming on in his legs and arms, but not in his back. He also has a sense of tingling and numbness in both extremities. Says, he is possessed at such times with great nervousness, and with feelings of fear. These symptoms are not connected with his gastric troubles—as he thinks. Pulse 104. December 7: Still an unfavorable report. Has had diarrhœa all this week. Feels badly in the forenoons and better in the afternoons. Tongue very much coated. Says one year ago it was quite black. December 12: Reports that on the 10th he felt miserable all day; on the 11th, decidedly better; woke to-day feeling quite well, but soon became upset again. Pulse 104. December 15: No improvement; feels nauseated. Pulse 116. Temperature has never been above normal. December 19: Not a good report. Pulse 120. On the 16th, 17th and 18th had more of the weak feelings and pains in his limbs. December 23: Pulse 120. Has feelings of great prostration. December 30: Pulse 104, weak and rather

irregular. His main trouble is a bad general feeling of inability to go out.

January 6, 1896: Not improving; some diarrhœa. Pulse 120. January 11: Has been a good deal better from the 6th to the 9th; but on the 10th, without any reason, all his old symptoms returned, with a good deal of insomnia and morning depression. January 16: Feels better. Pulse 102. January 23: Not so good a report. On the 17th had diarrhœa, following an occipital headache. Pulse 94. Has bowel trouble, with a great deal of flatus now. January 30: On the whole better, but feels his stomach uneasy all the time. Yesterday vomited once. Has one loose movement, with much wind, every morning. Still has aching in his legs and a tired feeling. February 7: A bad week. Pulse 92. Has one watery evacuation in the morning, after which he feels quite nauseated. February 14: Better again for a while, better than he has felt for a long time. Diarrhœa checked. March 6: Calls after this interval, having been on the whole much better. Pulse lower, though now 102. Diarrhœa much diminished. March 14: Much better; had only one loose movement the past week. (Continue treatment as of Graves' Disease.) April 20: Comes after more than a month's absence; has been a great deal better, and able to attend to business every day. Since taking peptonized milk his diarrhœa has ceased; only occasionally some nausea and dyspepsia. No more aches. Pulse still 110. May 5: Favorable report in general; but some gastric symptoms yet. Tongue brown coated. Pulse 100. June 2: Has been improving steadily; no more diarrhœa; no gastric uneasiness. Pulse 98. July 2: Been feeling well till lately. Found pulse 112; tongue coated. October 19: Been feeling very well, except during two weeks after shock of father's death. Pulse 86. Took peptonized milk all summer, till September 20. Since then has been on ordinary diet. November 25: His case shows the good effects of Graves' Disease regimen. He has been free from his pains, his prostrations, his digestive troubles, and able to attend steadily to business. Finds that he cannot take coffee in the morning, which is his weak time, but can take it with his evening dinner. Pulse 96.

December 30, 1898: Mr. S. has left off his medicines, and kept himself fairly well until about November, when his old gastric disturbances returned. Feels wretchedly on waking in the morning, with nausea. Has had a cough also for some eight weeks on rising, with such adhesive expectorations that he vomits. Pulse 112.

January 21, 1899: His digestive symptoms much improved. April 3: Comes with a return of all his old symptoms; has taken

no medicines for a month. Wakes in the mornings with gastric distress, uneasiness of the bowels, with irregular and loose movements, achings in his legs and arms. Pulse 120. April 8: Much better. Pulse 102. April 15: Better. Pulse 92. June 10: Calls, much improved in achings in his back and limbs; bowels quite regular. But his trouble now is a sense of gastric distress in the mornings. Tongue, as usual, much coated. Pulse 102. Says, he is growing quite fleshy. June 16: Bad report. Has had wretched mornings with his stomach, with severe bilious vomiting; head very light, with constant sense of gastric distress. Bowels not loose. November 11: Came last date in June. I gave him a thorough cleaning out with calomel and jalap cc. This acted strongly, with vomiting and purging, till second day. But on the second day he picked up, went on a fishing trip, and has been well ever since. Till lately, when he has morning depression, with a sense of general debility. Bowels regular. Pulse 104.

February 21, 1900: Calls for a return of his old typical morning depression, with more aches in all parts; pains down his legs and muscular weakness. Once he had causeless diarrhœa. Gastric symptoms not pronounced. Tongue, as usual, much coated. Says it has been black. Pulse 94. June 13: Has been a great deal better till lately, when his old digestive symptoms returned, with general aching. July 30: Again upset with some old symptoms.

January, 1901: Reports that he is now quite well, and entirely free from any dyspeptic symptoms. Pulse normal in frequency.

January, 1903: Regards himself wholly cured.

REMARKS.—The chief feature of his case was his obstinate gastro-intestinal derangements, which had the peculiarity of beginning suddenly one day, and then never varying in character for five years, but at no time presenting the slightest signs of an inflammatory character in either stomach or bowels.

CASE IV.—Mr. J. E. C. Æt. 42. Cashier.

Chronic gastro-intestinal troubles, with morning diarrhœa. Repeated occipital headaches. Persistent tremor of the right hand for six years. Extreme nervousness, with mental depression. Tinnitus and pain in the left ear. Pains in eyes and general wandering pains. Vesical irritability. Always worse in the morning.

This patient is a brother of Miss C., Case 12, with exophthalmic goitre.

June 13, 1894: Comes for great nervousness, frequent occipital headaches, achings down his spine, bad sleep; always feels worse in the mornings. He is greatly troubled with shaking of the right arm, which interferes with his handwriting and his signing checks. June 22: Better in his arm twitching, but his head continues to trouble him.

April 26, 1895: Comes with a story of feeling badly, and of debility; constant sense of pressure on the back of the head, and of general prostration. He sleeps well, but wakes with very bad feelings. Pulse 104. Complains of palpitation. May 8: Rather worse; aching in the back of the neck, with occasional flushing of the face; very much prostrated. Pulse 100. May 15: Feels a good deal better. May 28: Generally better but his head symptoms have returned, and he greatly complains of tremor in the right hand when signing checks. Has pain in the eyes. July 5: Comes now with a tendency to diarrhœa in the early morning. November 28: Very much troubled with the trembling of his hands. Now has palpitation. December 20: Feels great mental depression, with old aching at the nape of the neck.

January 1, 1896: Feels more tremor of the right hand; aching in the right shoulder, and aching in the upper part of the right leg, with general nervousness. January 27: More complaint of his head; more hand tremor, and more wandering pains. February 7: Feels on the whole better. February 14: Better, but troubled with wind in his bowels. March 30: Greatly troubled with indigestion and irritability of the bladder. Aching at the back of his head gone, but feels badly in his eyes. May 6: Variable report. Morning diarrhœa, with bad feelings in his head at that time. May 30: Diarrhœa checked; but he has morning pain in the bowels. June 22: Wakes too early, and with distress in his stomach. Pains again in the back of his head and neck. August 10: Comes with a story of repeated severe headaches, with prostration, and inability to sign checks. September 7: Improved by country trip, but still has morning headaches, and intestinal flatus; and now, in addition, tinnitus, with palpitation. September 11: Still has headaches, but not so severe. October: Feels generally better. Dr. Koller says his headaches have nothing to do with his eyes. Continue treatment as if for Graves'.

March 30, 1897: Has been much better through the winter of his headaches, while continuing the Graves' diet. Headaches returned, with occasional severe pains in the eyes. Tremor of the right hand continues. His old diarrhœa tendency in the morning is better, but he still has some flatulence and occasionally

some palpitation. April 27: Now comes with a story that for some days he felt as bad as ever, until he left off all medication. Some days after this all his old symptoms of morning headaches returned, together with his other troubles. Resumed treatment. May 31: Comes with a story of continued headaches, but always feels better after the blue pill. Hand tremor better. Does not have palpitation as before; no diarrhœa. Pulse 82.

May 30, 1900: Comes with all his old symptoms again. Tremor of the hand now more intermittent. Decided morning malaise. Diarrhœa better. Has a sense of falling while sitting still; has pain in the left ear. November 9: Complains of general debility and a sense of falling, always when sitting still, as in church. November 29: Still has symptoms of old nervous debility. He is now troubled with a ringing in his ears.

March 19, 1902: Has been on the whole improving, but is still troubled with a shaking in the right hand.

REMARKS.—This patient has a sister who had a temporary goitre, and whose history (Case XII of Class I) presents many similarities to his, except the tremor of the right hand. Though often troubled with palpitation, his tachycardia was not so continuous as in other cases in this list.

CASE V.—Mrs. C. H. Æt. 68.

Disease beginning with continuous nausea for two years, with progressive and extreme emaciation. Then severe but shifting pains in the scalp, in the ears (particularly in the left), with stiffness of the left neck muscles, stiffness of the tongue and jaws; pains in the knees and hips, and in palms of the hands. Marked tachycardia, 150-180. Total deafness of left ear. Aural vertigo. Transient diplopia, aphasia and delirium. Stomatitis. Phlebitis. Complete recovery for four and a half years, then fatal relapse.

April 11, 1896: This patient always enjoyed good health until two years ago, when she commenced with causeless nausea, in no way connected with eating. About a year ago she began to feel generally unwell. About November 1, 1895, she commenced to have positive, anomalous symptoms, consisting of general pains over her head and scalp, and marked tenderness of the external ears. She would then have violent neuralgic paroxysms over the head come on, with stiffness of the tongue and aching in her jaws. The following days there would be pain in the legs, especially in the knees and hips, though only on movement. Another symptom was intense pain in the palms of both hands;

but all her pains have more or less tendency to shift. After some improvement of the head pains, they have begun to occur in paroxyisms again during the past week, so that she is now entirely confined to her bed. I found her pulse varied from 140 to 150; temperature normal. She has no goitre whatever. The thyroid gland, if anything, is atrophied. No exophthalmos, or any other symptom about the eyes, but she claims she cannot read without producing trouble in her head. Extreme emaciation; some falling of the hair; bowels rather constipated; urine normal, no albumen or sugar. Examination of the painful parts showed no correspondence to true rheumatic inflammation, no tenderness on pressure of any joint, no swelling anywhere, and no redness, except of the ears. The tenderness on pressure was limited to the fascia of the muscles. There was nothing like peripheral neuritis, or true myositis; for the pains, which curiously stiffened the muscles and made them very painful on movement, in a few hours would shift elsewhere, always excepting the left side of the neck; nor were they affected by changes of the weather. The patient always felt worse every way on waking in the morning. Pulse always weak and very compressible. Lately she was much alarmed by an attack of vertigo. April 14: On the whole, relieved of her pains by the medicine, but to-day has had frequent attacks of greenish vomiting, with alarming sense of prostration, and attacks of vertigo which greatly frighten her. Pulse 124. April 15: Pulse 112. April 20: Pulse 100. Has some headache and slight return of pain. April 24: Feeling quite relieved of her pains. She has had no more turns of vertigo, but says she has more or less nausea all the time. Was a little wandering in her mind in the night, and forgot all happenings. Much gastric flatus, and still some pain on moving the knees. The peculiarity of her tongue is that it is stripped clean and red, pointed and inclined to be sore. April 26: Had a relapse of dizziness, with constant nausea. Pulse 100. April 29: No nausea, or giddiness. Pulse 102. May 3: Tongue red and sore. Complains now, mostly of nausea; knees still stiff. Pulse 96. May 6: Still complains of nausea. Says that she has had this nausea come on every morning for two years. May 10: Severe attack of nausea, with sinking; vomited twice. Rather serious condition. Nausea persisting. Pulse 140. May 14: Stomatitis worse. Pulse 116. May 16: Mouth better; less nausea to-day. Pulse 114. May 18: Not gaining; dizziness continues, and frequent nausea. Pulse 116. May 19: Passed a bad night from nausea. May 20: Had diarrhœa to-day, five movements. Some nausea yet, and some soreness of the mouth. May 21: The patient's emaciation has continued stead-

ily progressive, so that I have been compelled to have her padded with cotton batting to prevent the bones coming through the skin. The question of the cause of the vertigo led me to ask more particularly about her ears. She referred to the pains in both ears, spoken of at the beginning, with more pain in the left and going down the neck. The neck is still stiff, and she has to lie constantly on the right side on account of the pain in moving the neck. Bowels still loose, but she has less nausea, and no dizziness. May 23: More comfortable. Stomatitis, however, very troublesome. Pulse 108. She said that her vision was becoming disturbed, and she forgets words, and could not talk so well. May 27: Pulse 124. Has some pain in face and head. May 28: Had a remarkably good night. Pulse 108. No dizziness; less nausea, and mouth better. Says that for a long time she has felt stiffness of the tongue on protruding it. May 30: Pulse 106. Feels some pain and numbness in the right arm; some nausea and light-headedness. June 1: Still has pain in the right forearm, but other symptoms better, except progressive emaciation. June 8: Pulse 110. Begins to have some appetite. Can lie on her back now without dizziness. June 11. Feeling more comfortable every way. Pulse 110, but stronger and fuller. Wakes feeling better. For the first time in months read in a magazine. Reading has always brought on discomfort. Knees less stiff. June 15: Nausea unfortunately has returned. June 17: Nausea again, though not so pronounced; throat also sore; some increase in her muscular pains. Pulse 112, and small. June 19: Increased nausea, and sense of faintness. Pulse 114, and jumping. June 22: The extreme hot weather seems to have prostrated her. Pulse 112. Mouth again sore. June 27: Had a bad dream last night, followed by aphasia, which lasted five hours. No signs of paralysis. The aphasia was wholly motor. Pulse 114. July 6: On the whole better. Pulse 108, but feels weak. July 8: Feeling much better. Pulse 102. July 10: Feeling fairly comfortable, but very weak. Pulse 102. Ate with a relish a good meal of fish, lettuce and tomatoes. July 27: Has been on the whole more comfortable and stronger, but has some heartburn. July 30: Pulse 124. Has more nausea again, perhaps from this extreme heated time. August 3: Still complains of nausea. Pulse 108. Vomited twice. Now has pain above the right knee, and edema of that foot. Found she had phlebitis of the external saphena. August 31: Has been steadily improving throughout the month. September 16: After a calomel purge yesterday, pulse down to 92. September 18: Doing well. Goes down stairs now, and stays for the day. Pulse 96. September

23: Looking very much better. Stays down stairs all day. Has recovered her flesh. October 27: Has been improving steadily. Goes out riding and has been shopping. Still has some rheumatoid pains in the vastus externus. Occasionally feels light-headedness. No soreness of the mouth or throat. Has gained steadily in flesh. Pulse 100, and stronger. The hearing of both ears perfect. Tongue normal. No gastric symptoms whatever.

January 29, 1897: Comes to-day for the first time to my office, with excellent appearance. Knees still slightly painful, and some pain in the spine, and stiffness if she lies on her left side. February 15: Has been doing very well. Pulse 86. March 13: Has been doing well. Still has some pain in the legs, and cannot lie on her left side at night; has been walking a good deal this morning. Pulse 92. March 31: Comes feeling and looking well. April 13: About the same. Pains better, can turn in bed better. April 28: Pains much better; can lie on either side at night. Has a feeling of numbness in the toes, and some twitching of her fingers. Pulse 90, and good. May 17: Looks very well. Pulse 84. Still some pains in her legs and ankles after walking. June 11: Pulse 84. Feeling very well. Only complains of rheumatic feelings in her legs, but not in her joints. Numbness in the toes has gone off. October 26: Remarkable for her good looks; now weighs 121 lbs., within 6 lbs. of her highest weight in life. Has stopped all medicines, unless when she has some of her rheumatic pains.

February 25, 1898: The patient comes in remarkably good state of health. Has no trouble in her knees now, and but slight pain in her ribs on coughing. June 25: A few of her old pains in the left neck and ribs on taking a long breath. October 29: Remarkably well. Pulse 86. Has scarcely any pain anywhere. Drives her own horses now.

May 27, 1899: This patient is now the picture of health. She has gained in flesh and color. She has none of her old symptoms, except occasional neck pains in the morning. October 30: Excellent report. Looks blooming. Pulse 84. Occasionally has some pain in her back.

January 10, 1901: After apparent complete recovery from her illness, this patient now comes to me with symptoms of a return of her complaint, which progressed through the winter and spring, as will be hereafter described in the Fatal Cases. She died suddenly July 5, 1901.

REMARKS.—This patient had been a puzzle to her different medical attendants, as Graves' Disease was not once suspected,

because in her wasted condition the thyroid seemed atrophied, and the appearance of the eyes was normal. Her vertigo, diplopia and deafness, with other cerebral symptoms, had led to the diagnosis of brain tumor; her painful stiffness of the neck, with the tachycardia, to meningitis; her emaciation and constant nausea, to cancer of the stomach, etc. It was striking how completely she recovered from total deafness of the left ear when she regained her general health. Next to the obstinate derangement of the stomach, and following it in time, the most marked clinical feature became the great variety and distribution of her pains. On the other hand, notwithstanding steady perseverance in the line of treatment for Graves' Disease, she seemed for two months to grow worse, and her death at any time would not have surprised me; but I declined to change her prescriptions, and at last improvement began and continued.

I may add that I have never seen a patient, with wasting and marasmus such as hers, recover flesh and strength so completely; and yet that did not prevent her succumbing, after nearly five years, to a fatal return of the same disease.

CASE VI.—Miss C. B. Æt. 26. Schoolteacher.

Tachycardia for four years. Great nervousness. Neuralgic pains. Constant headaches. Pains and tinnitus in ears, with loss of hearing. Persistent gastro-intestinal derangements. Always worse mornings. Insomnia.

October 21, 1896: Comes to me for extreme nervousness, very frequent headaches, and various neuralgic pains, with a sense of weakness in her arms and legs. Pulse 120-140. November 7: On the whole better, but complains of constant pulsation in her neck and in her head, with pains at the back of the neck. Pulse 118. Has been losing flesh. November 25. Pulse still 120. But her general appearance better. December 26: Feels on the whole better. Pulse 102.

January 19, 1897: On the whole improving, but troubled with indigestion; headaches less, but looks thin. Pulse 106. March 1: Not so well. Pulse 124. Has been troubled with insomnia. May 8: Feeling much better. Pulse 94. Headaches greatly improved; not so nervous. June 4: Comes in a very weeping frame of mind, which would be easily mistaken for hysteria, but for the prolonged tachycardia. Much troubled with aching in the nape of the neck, and with general nervous weak-

ness. Has a throbbing in the head when lying on one side. Good deal of discomfort in her ears. Feels full after eating. Bowels inclined to frequent movement, but not loose. Pulse 102. June 29: Looks better, and has been better for a rest, but pulse 126. September 30: Been somewhat improved by summer vacation, but her symptoms are variable. Feels a sense of prostration and quickened pulse come on after eating. October 21: Feeling and looking much better. Pulse 104. December 7: About the same. Pulse 104.

January 27, 1898: Pulse 112. Occasional headaches. February 25: Comes with symptoms of gastric disorder, and feels generally weak; but pulse lower than ever, about 88. March 17: Feeling extremely weak and nervous. Pulse 90. Much troubled with acne. June 14: Constant tendency to morning headaches, and always feels worse in the mornings. December 1: Has been on the whole stronger, but very nervous and much troubled with a throbbing in her head. Pulse now 110.

January 17, 1899: Pulse 86. Feels so much better that she wishes to leave off treatment. March 8: Has had more headaches, and complains a great deal of tinnitus, and occasional palpitation, with insomnia. Pulse 120. May 20: Has been a good deal better. Pulse now 100. Complains of a great fulness in her ears, and right ear has some loss of hearing. June 29: Thinks that she is a great deal better. Pulse 102. October 3: Better. Pulse 92. But still complains of loss of hearing. December 9: Has been doing quite well. Pulse 98. Her ears much better.

January 2, 1900: Has been doing pretty well, but pulse 100, and still has a tendency to headaches. April 7: Pretty fair. Pulse 100. Some palpitation after meals. June 2: Much better.

October 11, 1902: Since last date has continued to be in very fair health, with normal pulse, averaging 80.

REMARKS.—This case could readily have been diagnosed by some medical men as one of hysteria, and by others as neurasthenia, and she would not have derived any benefit from the usual prescriptions for such states. Her persistent tachycardia gave me the first clue to the nature of her complaint; for otherwise, a number of the accompaniments were lacking. She never had relief, except from intestinal antiseptics.

CASE VII.—Miss E. P. Æt. 20. A sister of Miss M. P. (Case IX.), who had goitre.

Constant migrainous headaches, with pain in the neck. Pains in the eyes. Pains in the ears. Persistent tachycardia, and palpitation. Vertigo. Insomnia. Tendency to abasia. Worse in the mornings.

November 23, 1897: Patient somewhat anæmic, first consulted me for headaches of two months' standing.

May 9, 1898: During the whole past winter she has had much gastric discomfort, with headaches, and complained a great deal of aching at the nape of neck. May 11: Still continues to have her neck ache, so that she feels discouraged with it. May 27: Writes that she suffers a great deal of pain in her neck, and often cannot sleep from it. Has a good deal of indigestion, with constipation. October 15: This patient, in general, with conditions much like her sister, still has her headaches. Pulse 100. A good deal of gastric dyspepsia. Pain also in the right hypochondrium, and pains in her ears, with fullness and throbbing in them. November 25: Comes for headaches on the vertex, and down the neck. Sleep very poor. December 5: Headaches better, but neck ache continues. Pulse 110. Says she is troubled with feeling her heart beat.

January 14, 1899: Writes that for three weeks she felt better than for over a year, but that the pains have returned on the vertex and neck, and over the eyes. Worse after waking in the morning. Often feels nauseated and has constipation. February 2: Comes with a disappointing report; is nauseated, and has frequent palpitation, bad pain in the eyes, headaches, nervousness and low spirits. Pulse 100. February 14: Considerable gastric disturbance. Pulse 100, and slightly irregular. February 18: Better generally, but some wandering neuralgic pains in sides and bowels. February 22: Pulse quite irregular. Total anorexia. Has some blur before the eyes, and still the pain in the back of the neck. March 6: Inclined to headaches in the morning, with nausea. March 15: Continued nausea; tongue very clean. Headaches (occipital), with tenderness of the eyeballs on pressure. Fits of much depression. Pulse 94, and irregular. March 25: Feeling better. Pulse 85, but still irregular. March 29: Not so much headache, but nausea very persistent. Looking quite anæmic. April 6: Has had considerable gastric pain, also pain in the ears, and some palpitation. May 8: Writes from the country that she has been better of the neck pain and in most other respects. December 17: Writes that she has been much troubled with gastric flatulence; pains in her neck and her ears; rapid heart beat, especially on waking in the morning, and with some nausea the most of the time.

January 16, 1900: Much troubled with her stomach and fre-

quent headaches; poor sleep; anorexia. February 22: Stomach troubles increased. Occasionally headaches for two days at a time. February 24: Not much change. Pulse 110. Gastric pain on empty stomach. March 5: About the same. Pain in the stomach persists. March 9: Pulse down to 84, but the dyspeptic symptoms continue, with occasional dizziness. April 9: Pulse small and weak, 114. April 30: Has had bronchitis, with fever, which kept her in bed for about two weeks. Comes now with same old story of constant headaches. Looks pale. Great gastric flatulence. Pulse 110. May 4: No change. Pulse 96. May 18: Still gastrodynia, headaches, etc. Pulse 130. After eating her heart goes very fast, she says. June 15: Pain in head less severe, but still aches every morning on waking, and then becomes better. Neck aches, especially in the morning. Much gastric flatulence. July 5: Has been on the whole better. November 18: Same old symptoms. Pulse 110 to 120. November 23: Symptoms continue, but pulse down to 88. December 3: Has lately been troubled with diarrhœa. December 30: Has felt much better; but recently more palpitation, with flatulence, after eating.

March 1, 1901: Has been a great deal better since last date. March 11: Headaches better; flatulence better, but recur. April 8: Headaches most at the time of her courses. Feels very nervous and tired. Aching in the ears, especially the right one. July 17: Has attacks of faintness. On Sunday her heart beat so rapidly she got faint and had to leave the church. When she wakes in the morning her heart beats very fast. Auguts 20: Writes that she has been very miserable with neck and back aching, and with flatulence. She has had attacks of throbbing pains in the ears. While walking in Boston, felt as if she were going to fall. November 12: Fears going alone lest she should fall. Has severe attacks of palpitation on waking. Pulse 126. Occasionally has pain in the right ear. Inclined to constipation. November 16: Comes to-day looking and feeling much better. Pulse 92. Has sudden attacks of blur in the eyes. Afraid to go alone from attacks of faintness. December 19: Has attacks of chilliness at night, and still many of her old troubles.

REMARKS.—As above noted, this patient's sister once had goitre. Besides the tachycardia, her headaches and digestive disorders proved extremely uncontrollable, while her other symptoms closely resembled her sister's, except that the thyroid never enlarged.

CASE VIII.—Miss M. M. Æt. 21. Healthy looking young woman.

Sudden beginning of symptoms of great nervousness, with tremors and sense of fright. Tachycardia. General prostration. Weakness of the knees. Gastric distress, with nausea. Vesical irritability. Sweating.

February 5, 1898: She states that she always had good health in the past, except painful menstruation, which had been relieved by an operation, probably for stenosis of the cervix. Through last summer she had been unusally well, having been at the seaside, when suddenly, while at the table three months ago, she had an attack of palpitation come on—without any warning—accompanied by a feeling of great weakness and nervousness, as if she had had a great fright. Ever since then she has had continuous nervousness of this kind, and she remains, as she expresses it, "In a constant state of nervousness," most apt to occur while eating, with a sense of inward chills and general trembling. This does not affect her handwriting, but the feelings of tremor, with a sense of weakness of the knees, is always constant. Since these troubles have come on, she has become very dyspeptic, and frequently has a feeling of nausea, so that now she lives mostly upon broths or other liquid food. Her bowels are regular, but she has increased vesical irritability; no itching; no loss of hair; no sweats, except one day after the weak feeling. Has had no history whatever of shock, or fright, or mental strain. Never had rheumatism. Pulse 114. Eyelids on closing very tremulous. No goitre. Says that she feels that her eyes are too full and staring. No history of migraine; no pains and no cramps. February 12: Comes much improved in her digestion. But still has palpitation, pulse 100, and is nervous. February 21: Much better of her digestion, also of her nervousness. But has feelings of great weakness and prostration come on. March 12: Not so good a report. Has had nausea; more sense of her frightened feelings, with a feeling of tremor. March 25: Is evidently improving, but says she still has nausea. April 14: Says she is more nervous and frightened than ever. Ascribes her nausea entirely to her nervousness. Says that she now has sweats at night.

This patient ceased attendance after this date on the plea that her nervousness was not relieved.

REMARKS.—It is interesting to note the abruptness of the first onset of the complaint in this patient, parallel to the experience of Case III, which also began after a single meal. She expressly

denied having had any mental or other exciting cause for the first attack; nor could she account for it by what she ate on that occasion. Such an attack could not be termed a gastric crisis, for it persisted too long afterwards.

CASE IX.—Miss L. K. W. Æt. 32.

Severe migraine of many years standing. Tachycardia. Chronic gastric disturbance. Persistent nausea. Tinnitus. Pain in left ear. General tremor, and tremor of right hand. Weakness of the knees. Vesical irritability. Loss of hair. Always worse mornings.

October 14, 1898: Comes with the statement that when 14 years old she had an attack of great trouble with her eyes, when she had constant flashes of colored light, so that she could not see, accompanied with severe headaches. This condition of her eyes continued for several months. Then another attack of the same kind three years afterward; then two more also, at three years' intervals. Then again another after seven years' interval; and now another after two years, the attacks gradually lessening in severity. Only one eye is attacked at a time. They first came on with the beginning of the menses. She says she has hemiopia with the affected eye. She becomes very dizzy, and also when she is getting well, she notices that the field of vision is contracted, and the discrimination of colors deficient. The other symptoms are those of persistent tachycardia, chronic stomach trouble, and frequent pains after meals. But the most prominent symptom is nausea, especially upon nervous excitement. She has pain in the left ear and behind it, with throbbing, which is worse at night; no other pains. She has general muscular tremors, especially in the hands, more in the right hand, so as to affect her writing; weakness of the knees; great irritability of the bladder; at times a great falling of the hair. Pulse 118, very small and weak. No heart murmur. Bowels natural; menses regular. Much troubled with cold feet. Always worse in the mornings. Says that her attacks always begin on the same date in the year; that she invariably emaciates during them. Though her mother never had migraine, her father was a martyr to it every week until he was 40 years old; also his father has sisters with it and most of the sisters' children (cousins of this patient) have it, some of them very severely. November 16: Heard from her that she was doing finely, better than she has been for years. December 7: Report that she has been improving steadily, only two headaches since October 14, and they were not as severe as usual.

January 21, 1899: Comes to-day with a story of continued and great improvement in all particulars; has only occasionally a spasmodic cough. May 15: Her father writes that she was gaining steadily till about three weeks ago (about the usual time of the year for her to have a breakdown), when she began to have spells of being very tired; no cough; no tremor; appetite good. May 30: Father reports that the prescriptions do not seem to relieve her. She is not so tired as she was, but has spells of being so exhausted that she cannot seemingly hold anything in her hands. She is greatly troubled with tinnitus.

May, 1901: Heard that this patient had now entirely recovered.

REMARKS.—This is one of many patients in whom migraine—like headaches—are a leading symptom throughout, and the relationship of which to the disease I discuss elsewhere.

CASE X.—Miss G. H. Æt. 24. Schoolteacher.

Tachycardia of four years' standing. Pains in the heels, in the tips of the fingers, in the cardiac region, in the throat and in the ears; cramps in the calves. Tremor of the hands and legs. Paræsthesiæ. Headaches. Nervousness. Pronounced gastric and intestinal derangements. Vesical irritability. Worse in the mornings.

May 15, 1897: Brought by Dr. Kyce, of Port Oram, N. J. Three years ago this patient was attacked with a pain in both heels; then in the feet; then cramps, into ridges, in the calves; then pain in the tips of the fingers of both hands. After this, frequent headaches, generally occipital; also attacks of severe gastralgia; pains in the cardiac region; tremor of the hands, interfering with her writing; tremor of the legs in walking; paræsthesiæ and numbness and tingling in the feet on standing. Knee jerks normal. Eyelids somewhat widened, but no exophthalmos. Says she has a feeling of tenderness in the throat. lately has had pain in the right ear. Eyelids on closing very tremulous, especially the left. Pulse 140. Dr. Kyce says that for months he has never found pulse below 120; extremely nervous. December 28: Comes to-day with a story that she was much benefited for a time, but has lately rather retrograded. Pains in the feet, in the heels and in the calves better, but is still weak in her legs. Persistent nausea. Bowels for a time alternately constipated and then loose; recently more regular. Her headaches no longer occipital, but frontal and in the eyes. Often quite pronounced pain in the ears, more particularly in the left; pains in the tips of her fingers, if she raises her arms,

or lets them hang down. A good deal of vesical irritability. Hands and feet perspire; no itching. But she has frequent pains in the cardiac region. This patient considerably improved at first, but heard from her doctor a year afterward that it was impossible to get this patient to follow treatment, and the last he saw of her she was no better.

REMARKS.—The prolonged tachycardia, the tremors, the excited manner and wilfulness of temper, the peculiar pains, the headaches and characteristic disturbances of stomach and bowels, were all as typical as they could be of Graves' Disease; and yet at no time for at least four years was the thyroid even tumified.

CASE XI.—Miss A. R. Æt. 40.

Tachycardia, with pronounced gastric symptoms. Colored spectra and eye pains. Pains in various muscles, in toes and tips of fingers, ears and neck. General and local tremors, especially of the right hand. Weakness of the knees and of the voice. Paræsthesiæ. Emaciation. Worse mornings.

December 13, 1898: Sent by Dr. A. S. Dana, of Bronxville, N. Y. About a year ago, while nursing her mother, who had a fatal illness, she began to be much troubled with her stomach, with attacks of flatulence, and blue and black specks before her eyes. Then palpitation set in, and has continued ever since, especially after eating. Then pains in the muscles, and in her knees, and especially in the toes, also in the tips of the fingers; also pains in the right ear, which became very painful to the touch, and with pains behind the ear. She also had tremor of of the limbs, and weakness of the knees, and unable from tremor of the right hand to sew. Loss of flesh equal to 25 lbs., which is marked in a patient never fleshy. No headaches; no itching; no irritability of the bladder; but bowels irregular. Eyelids very tremulous, but no exophthalmos. Thyroid appears to be atrophied. Pulse 140. Always feels worse in the mornings. No heart murmur.

January 10, 1899: On the whole improvement. February 21: Reports that she feels some stronger; pains much less; palpitation less, but much troubled with coldness of the feet and hands, and has color spectra. Pulse 120, very small. Considerable gastric disturbance; bad taste in the mouth. March 24: Report of general improvement. Muscular pains, wandering in seat, but much less; less pains in the fingers and toes. Says her right eye seems to bulge if her heart palpitates. May 1: General improvement. Pains less; palpitation less; not so cold

in the feet and hands; instead, a change into a sense of burning of the feet. June 5: Bad report. Pulse 130. Has had diarrhœa. Voice very weak; pain in the right ear; great many colored spectra. July 7: General improvement, though the eye symptoms are there yet. Pulse 124. August 7: General improvement. Pains less; also less in the ears. Feels stronger; fewer muscæ volitantes. Pulse 114. November 13: General improvement. Gaining in flesh, and sleep good. Palpitation less. Pulse 104. Muscæ not so pronounced. Constipation less. December 21: Comes discouraged. Pulse 130. Ear pains worse, also in the chest; pains in the eyes; very weak.

June 23, 1900: Much better. Pulse 98. But complains greatly of cold feet.

March 5, 1901: On the whole stronger, but all old symptoms still present. Patient ceased attendance.

REMARKS.—In this patient the thyroid seemed to be much smaller than normal, but the symptoms were as characteristic of Graves' Disease, and of no other complaint, as they well could be.

CASE XII.—Miss K. Æt. about 30. Schoolteacher.

Tachycardia for four years. Prolonged gastric disturbance. Tremors. Weakness of the knees and general prostration. Pains in the ears. Bulimia. Insomnia. Worse mornings.

January 28, 1899: A healthy looking young lady, who says she is quite subject to malaria, with afternoon attacks. While in the country lately for some two months or so, she has felt very weak and badly in the mornings, with violent attacks of palpitation. No other special symptoms, except a sense of inward tremor, rarely in the hands, but in the knees. Some sensitiveness lately in the left ear. Pulse 100. February 6: Better generally, but palpitation, with flatulence, frequent. February 18: General improvement. Morning sensations better. Pulse 100. February 23. Change in symptoms. The attacks of depression coming on very suddenly, also a general weakness. A very disagreeable sense of hunger, which comes on suddenly. March 3. No improvement. Pulse 110. Complains of weakness, and sleeps very heavily. She is troubled with palpitation and throbbing in the left ear at night. March 21: On the whole better. Pulse 92. April 19: Was doing very well, until from over-fatigue of moving, all her old symptoms returned; sinking at the stomach, flatulence, palpitation, with attacks of intense prostration. Pulse 110. June 3: Most of her symptoms gone, except palpitation. Pulse 100. July 1: Been feel-

ing much better of late, except when feelings of weakness come over her. No headachs; no neuralgias, but says she has attacks of blindness when arising in the mornings. July 15: Attacks of dizziness; occasional palpitation. September 29: Felt better in the country, but begins to feel weak again. Says that she has been losing flesh steadily.

January 14, 1901: Has been better. Pulse 86. But is much troubled with nausea. April 9: Nausea continues. Cannot take solid food without causing palpitation. Pulse 82. April 24: Constantly troubled with gastric weakness; unable to take solid food. Palpitation at night. Pulse 100. May 29: Looks emaciated. Still unable to take solid food. Pulse 112. June 7: Better. Pulse 96.

February 20, 1902: Comes for a diarrhœa of four days standing. Pulse 110. Been on the whole better. May 28: Diarrhœa was at once stopped by a blue pill, but digestion very weak. Often has palpitation. Pulse 90, and weak. May 9: Was better for a while; but now has attacks of palpitation and nervousness. May 26: Nervousness and palpitation better, but has been very prostrated. Chief complaint now anorexia, insomnia and bad dreams. Pulse 110, and very small. November 8: Passed the summer fairly. But the old conditions persist in one form or another. Pulse 110, small and weak. This summer for the first time she has had a great many headaches. Some tinnitus in her left ear.

REMARKS.—This case illustrates the intractable nature of the gastric derangements of some of these patients, of which Case VII is also an example. The variety in the clinical manifestations of Graves' Disease, however, is shown by the constant association of migrainous headachess in Case VII, while this patient was entirely free from any headaches for three years, after which they began to appear.

CASE XIII.—Mrs. J. W. Du B. Æt. 48.

Tachycardia, with attacks of very rapid breathing for seven years. Spasmodic tic. Weakness of the knees. Pains. General tremors. Insomnia. Intestinal disorders. Functional deafness.

May 12, 1899: Brought by Dr. J. B. Peters, of Walden, N. Y. This patient has had for some seven years peculiar attacks of dyspnœa, with very rapid breathing. These attacks would last for several weeks, and then would improve. But for the past winter they have been very continuous. She was long subject

to migraine, with many colored spectra in the attacks. These have now ceased. Her mother was very migrainous. Three years ago she lost the hearing in her left ear, without any apparent cause. She has now occasional attacks of spasmodic tic in the left eyelid, and in the left muscles of the face. Feels very weak in the knees, with general tremor. Rheumatoid pains are frequent in various parts of the body, especially in the left leg. Sleep is very poor. No evidence whatever of thyroid enlargement. Her chief complaint is intestinal flatulence, and she maintains she is always better when her bowels are loose. She does not lose her voice, but her throat feels choked when she has her palpitation. Pulse 130-140. October 14: This case is of interest as one of great improvement in the space of five months, since May 12. She went for two weeks without palpitation, which has not returned badly, but she has had greater weakness in her legs during the summer, with great intestinal flatulence. Her attacks of spasmodic tic have increased in frequency, completely closing the left eye, with distortion of the face, and sense of construction from the neck to the forehead. A singular feature is that when she has palpitation now she has total deafness come on in her well ear, the right. She is beginning to be quite insomnic again.

NOTE.—May, 1900: Heard from her doctor that she was gradually getting better.

REMARKS.—The tachycardia of this patient was very pronounced, yet the attacks of rapid breathing seemed to be an independent element. I have noted a case of this kind, like a respiratory crisis, also in a patient with exophthalmic goitre. Her attacks of spasmodic tic were as severe as any which I have seen, greatly distorting the left side of the face and totally closing the eye. The connection of deafness with palpitation is interesting.

CASE XIV.—Mrs. A. C. Æt. 36.

Tachycardia. Headaches. Vertigo. Pains. Tinnitus of left ear. General tremors and morning shaking of right hand. Weakness of knees. Loss of hair.

August 1, 1899: Came to see me in consultation with Dr. J. O'Leary, of this city. This patient has had migraine since childhood. Mother very subject to it; also two brothers, but neither of her two sisters had it. She is much troubled with constipation. Her headaches have grown worse and more frequent. She has incessant and annoying tinnitus in the left ear;

has had rheumatoid pains in the right knee and left shoulder, and complains of constant shakiness in and weakness of the knees and legs. Her hands shake so she cannot write. Attacks of dizziness come on in the morning. She has been much annoyed by the falling of her hair. She has a sense of constriction in her throat; her voice sometimes gives out altogether. Her eyelids tremble moderately when shut. Pulse 106. Cannot sew till evening. August 21: Attacks of dizziness continue, but pulse now down to 86. The patient is very irritable, and disinclined to follow treatment.

REMARKS.—This patient was quite surprised when asked if the tremors she complained of were worse in the morning, for she could not understand why she could sew only in the evening. Her physician afterwards told me that her mental state was changing into extreme irritability and wilfulness.

CASE XV.—Miss J. M. Æt. 38.
Tachycardia. General weakness. Weakness of the knees. Headaches. Tremors. Pains. Diarrhœa. Worse mornings.

January 15, 1900: Has been troubled for over a year with symptoms of prostration, palpitation, headaches, a sense of inward tremor, some tremor of the eyelids, and always worse in the mornings. Pulse 126. Other developments are slight. February 7: On the whole better. Pulse 98. Has attacks of causeless diarrhœa come on in the night, without any pain or other symptom. Some pain under her left shoulder blade. February 24: Better. Pulse 84. But the pain under the left shoulder blade persists. May 10: Comes improved on the whole, but all symptoms are still there. Complains of weakness of the knees; occasional palpitation; occasional diarrhœa, and still always worse in the mornings. Tremor of the eyelids less, and less general tremor. Her chief complaint now is the pain under the left shoulder, and in the left side of her chest.

REMARKS.—The history of her symptoms occupied about two years, and were very uniform in their character. This feature about Graves' Disease is almost pathognominic. However prolonged the story, the symptoms remain consistent with Graves' Disease only, even though the case, as in this instance, was a comparatively mild one.

CASE XVI.—Mrs. S. A. S. Æt. 40. South Norwalk, Conn.
Persistent tachycardia, beginning as paroxysmal. Severe mi-

graine, with paræsthesiæ. Tinnitus with deafness. Tendency to abasia.

June 1, 1899: Comes with her physician, Dr. W. B. Bean. About two years ago this patient began to have attacks of paroxysmal tachycardia. They began with a sensation in the head, as if she were about to fall, not particularly to one side of her. Then her heart begins to palpitate, and, Dr. B. says, may run up to 160. With this, she has a feeling running down her left arm, which becomes powerless. These attacks may last two days. Now, she can know of their coming on for one or two days before, by the change in her complexion, when (she says) "She turns green." From the beginning of these turns, she had a roaring in the ears, which has never left her, but has now changed into continuous singing, most pronounced in the left ear. I found that a watch was heard only about two inches from either ear. During these attacks she is generally troubled with muscæ, generally dark colored, and with a flow of tears, also a sense of aching in both hips and both knees. She has a good deal of gastric uneasiness after eating, but no nausea or pain. Pulse on examination is 80, and in the interval, Dr. B. says, it is normal. One brother she speaks of having died of heart disease at 25, and one sister also died at 25. Her mother died suddenly of apoplexy. Her father and one brother had hemiplegia. Sometimes these attacks come on in the night, and she feels as if she were about to die, but is not alarmed. September 11: Interesting story. The blue pills caused her to "feel splendid," better than any other effect. Other symptoms: She now has no numbness in the left arm; weakness gone; pain and aching in hips and knees gone; noises in her ear much diminished; muscæ gone, except lately in the paroxysms of the palpitation they came on as much as ever. But now evidently not like during the attacks of paroxysmal tachycardia. Her main trouble now is gastric uneasiness after eating. She does not feel worse in the mornings. She often has tremor when she feels badly, especially about 3 P. M.

February 2, 1900: Heard from her brother that she is much better; only had one attack of tachycardia. May 17: This case is now fully like Graves' Disease, with persistent tachycardia. Her pulse to-day is uncountable—feeling more like a continued thrill. Constant tremor of the eyelids. All her other symptoms continue to come on, especially the tendency to fall.

January 15, 1902: Heard that she is entirely recovered by the persevering use of the treatment recommended. Her deafness has completely passed off.

REMARKS.—I at first regarded this patient as a subject of severe migraine, with paroxysmal tachycardia as one of its accompaniments, for her pulse was normal in the intervals. A year after her first visit I found her with marked persistent tachycardia, and both her tinnitus and deafness very great. I recommended continuance of treatment, with the result of entire recovery in about eight months, both of her general health and of her hearing.

CASE XVII.—Mrs. W. A. C. Æt. about 35.

Tachycardia. Diarrhœa of four years standing, with gastric accompaniments. Emaciation. Attacks of unconsciousness, with anomalous nervous symptoms. Vertigo. Various pains. Cramps in left side of neck and limbs. Worse mornings.

June 21, 1899: Says her bowels have been troubling her for about four years, with early morning diarrhœa, watery passages and much flatulence. Better in the afternoons. She has a good deal of nausea. Pulse 100. Her most prominent difficulty is attacks of what she terms "flashes," or a feeling in the head—starting from the stomach and going up the throat—her jaw then drops and she becomes unconscious. With this aura she feels as if her whole body had lost sensation, except in the joints. As she expresses it, "She feels as if she were all joints." At other times she has a strange feeling come on, with tight sensations about the jaw, which drops. She is then obliged to sit down at once. These attacks come on now about every three weeks. Sometimes they wake her up at night with their onset. She has cramps in the left side of the neck, in the right arm and in the left leg, also much nocturnal aching of all the extremities, etc. She has flashes of rainbow colors till she becomes blind. Has frequently had scotoma in the right eye. She has a sister much troubled with migraine. Her father's mother had migraine severely, but her own mother (who comes with her) is healthy and perfectly free from it. July 31: Mrs. C. comes now with a story of improvement. Has had diarrhœa only once. Nausea is much better, but she still has dizziness. Had one of her unconscious attacks yesterday, with a relapse of the diarrhœa. Sleeps much better; much less nocturnal aching. August 7: Bowels again very troublesome. August 23: Comes now with improvement in all respects. She is sure that all her nervous symptoms seem allayed by the antiseptics. September 24: Comes looking remarkably better; has gained in flesh, and is less anæmic. Diarrhœa stopped, and all her nervous symptoms

are improved. Has had only one attack of unconsciousness, just after the last date. October 25: Somewhat troubled with stomatitis. She has had no bowel trouble, but has had a good deal of dull headache lately. December 1: General improvement.

February 28, 1900: Very favorable report. Better than she has been in 18 years. Has no palpitation now; occasionally intestinal disturbances. April 30: She got along very well until she was over-fatigued, since then she has had attacks of palpitation, with dyspnœa. June 5: Comes with very encouraging report. Remarkably well, she says, for her. July 10: Troubled with dizziness; and sometimes her bowels are too loose. September 10: On July 14 she had one of her attacks, in which she remained unconscious for over twenty minutes. Bowels is loose. Occasional headaches, but otherwise feeling better. September 21: Bowels much better, but some gastric flatulence still. October 15: Bowels still loose. November 22: Still the watery diarrhœa and some of the old digestive symptoms. Feels empty shortly after eating. Some wandering pains in the muscles, especially in both hips.

February 27, 1901: Remarkable improvement during the last three months. Looks better in every way. No headaches; none of her old symptoms. Heart very quiet. She has some looseness of the bowels occasionally, always early in the morning.

February 15, 1902: Mrs. C. feels entirely recovered.

REMARKS.—This patient's history presents a picture of the great variety of nervous derangements which may be occasioned by a toxæmia of intestinal origin, for all her diverse symptoms were closely associated with the condition of her bowels, and were as distinctly benefited by antiseptic intestinal remedies Her tachycardia and palpitation always improved after a mercurial laxative. The characteristic tremor of Graves' Disease was absent in this patient, but the four years persistent painless diarrhœa, with severe nervous, rather than intestinal, accompaniments, and the recovery from all these, along with the subsidence of the cardiac symptoms upon the cure of her gastro-intestinal derangement, fully justifies her inclusion in this list.

CASE XVIII.—Miss M. F. Æt. 24. Lakewood, N. J.

Tachycardia. Intestinal symptoms. General weakness. Nervousness. Tremors including right hand. Headaches. Vertigo. Worse mornings.

May 17, 1900: This is a case of intestinal indigestion of long

standing; obstinate constipation; unable to take any starchy food. Pulse 100. May 28: Complains of general malaise, and a tendency to weakness, particularly in the hands and arms; much troubled with headaches. Pulse 116. July 14: Has been doing pretty well, but the symptoms continue. September 29: Has been spending the summer in the Adirondacks, and feels stronger, but has been greatly troubled with sick headaches, with symptoms of intestinal indigestion. Tires easily. Found pulse 130. Sometimes has troublesome palpitation. Feels badly in the morning, and especially headachy. No pains; no ear symptoms. Eyelids very tremulous; sense of general inward tremor; occasional tremor of the right hand. She has three sisters who do not have migraine, but her mother was much subject to it. October 13: On the whole better, but feels weak. Pulse 126. November 5: Her sister writes that she does not feel as well; is frequently dizzy when she bends forward. Feels her head not clear when she writes. She is very nervous; easily tired, and constantly troubled with intestinal discomfort and continuous constipation.

REMARKS.—This patient was under my observation for only six months. But though she improved in many respects, no impression was made upon her tachycardia during that time. It was difficult to have her observe dietetic rules.

CASE XIX.—Mrs. W. A. M. Æt. 46.

A case without tachycardia, but with other symptoms of Graves' Disease. Gastric derangement. Nervousness. Headaches. Pains. Pains in left ear, with tinnitus. Vesical irritability.

Mrs. M. is a sister of Miss O. B. (Case XXV), who has Graves' Disease, with pronounced exophthalmos and goitre.

March 28, 1900: Mrs. M. comes on account of much gastric flatulence, with headaches, nervousness, pains in different parts of the body, vesical irritability, and a sense of pronounced inward tremor. April 14: No improvement. Very much troubled with her digestive symptoms. April 24: Not much improved, except appetite better. May 1: Not improved. Now considerably troubled with pains behind the left ear. May 21: Still very dyspeptic. Says her gastric symptoms were actually relieved after taking lobster salad and strawberry shortcake! Still complains of pain in the left ear. Feels very nervous. Sometimes has pains shooting from the left eye upwards. Always feels better after taking a blue pill. October 2: Nervous-

ness increased. Pain and tinnitus in the left ear; shooting pains in different parts of the body.

December 20, 1901: Patient gradually improved. But at this date I was called in consultation to see her, in an attack of acute pneumonia, from which she died eighteen hours subsequent to my visit.

REMARKS.—This case is interesting as the one exception in this list of absence of tachycardia, corresponding in this respect to Case XXIX of those with goitre. On the other hand, her sister, as above noted, has pronounced exophthalmic goitre, and no one could doubt that both had the same disease.

CASE XX.—Mr. J. C. D. Æt. 33. Express clerk.

Tachycardia. Gastric disorder. Bulimia. Nervousness. General tremors. Tremor of the right hand. Weakness of the knees. Chronic migraine. General itching. Vesical irritability.

October 1, 1900: Sent to me by Dr. George W. Bogart. He gives a story of chronic migraine. With the migraine he had attacks occasionally of severe protracted vomiting. This was followed by a very troublesome pruritus, for which he was unavailingly treated by several physicians, till Dr. Bogart cured him. Since the subsidence of the pruritus he has had gastric disorder, with much flatulence, but with attacks of hunger. At times he can eat without any trouble. Had his stomach washed out, but without any good result. Complains of intense nervousness, with general muscular tremors, especially of the right hand. Constant irritability of the bladder. Found his pulse almost uncountable, and irregular, the beats averaging 140. No sign of goitre or exopthalmos. Sometimes troubled with muscæ volitantes. Tongue coated. Often feels very weak in the knees. No pains of any kind. Now bowels constipated. Mother died of phthisis at 44, but suffered from migraine. He has one brother who suffers very severely, and faints away during the attacks; and another brother who does not suffer so severely; also a sister badly; but growing less as they grow older. Father never had it. October 22: Reports that he has very greatly improved. October 28: Great improvement until this week, when he had a relapse of indigestion and headaches, and a return of the tachycardia. Pulse now 94. Irritability of the bladder better. November 25: Comes with a relapse. This patient's habits are very irregular, especially in the matter of diet. Pulse 140. Is much troubled with headaches, and has constipa-

tion. The itching of the skin has returned, and the irritability of the bladder, as has also the shaking of the right hand. He ascribes it all to a change of occupation, as clerk at a desk, where he is standing three hours at a time. December 9: Much better. Pulse 110.

May, 1902: Have heard from Dr. Bogart that this patient has run down, due to his irregular living and dissipation.

REMARKS.—This patient improved greatly under diet and treatment; and then equally grew worse upon his refusal to continue his regimen.

CASE XXI.—Mrs. J. G. A. Æt. about 40. Wife of a physician.

Tachycardia. Mental depression. Perspiration. Loss of hair. Pain behind and in left ear. Pain in finger tips. Pain in throat. Muscular stiffness. Occasional causeless diarrhœa, with intestinal distress. Vesical irritability. Weakness of knees. Abasia. Worse mornings.

August 13, 1899: Her husband writes to me:

"That the first symptoms were noticed in 1895, after the birth of her first child. She became very nervous, easily put out and worried, and apt to be very depressed, and only slowly recovered from this condition, and not until the summer of 1897 was she herself again. In September, 1898, she was a good deal reduced by lactation. There had been for two months before this a great liability to perspire. This perspiration became excessive, a dozen or more attacks during the course of the day; with a cough, mucous expectoration, and tachycardia, pulse ranging some weeks between 90 and 110, with no relationship between the pulse and her temperature. She then developed symptoms of tuberculosis of the right apex. Her mental depression increased. Scant bacilli were noticed in her sputum about November 20. She then went to Saranac. She had fleeting pains over her chest, joints, etc. While at Saranac she began to gain in flesh, 28 lbs. in two months—½lb. a day! She is now less nervous, and the bacilli have disappeared. In February of this year (1899) many of the symptoms to which you call attention were very marked, the perspirations at times excessive. Her hair since December has been falling out in great quantities. Her frequent complaint has been: Pain behind and in the left ear, stretching back to the occipital region. Numbness and soreness of the finger tips have been often noticed. There are no tremors, however, of the right hand. Sleep has been disturbed; depression has been markedly severe in the early morning; has

a series of symptoms also of the rheumatoid type. Frequently complains of muscular stiffness, with pains in the right shoulder, stiffness in the thighs and groins, more marked on the left side. Another pain in the inner side of the right chest, with pain in the throat. With all this multiplicity of pains and depression, her digestive system has given very little trouble for some years. She has had a distinct tendency towards constipation, but in November and December was troubled with looseness of the bowels, coming on without obvious cause. Since then, although her bowels have been in excellent order, she complains of an ill-defined distress in her bowels coming on suddenly, and then passing off without any passage. She complains occasionally of these feelings coming on suddenly in the middle of the night. She described them as the most terrible of all, and fears them greatly, stating that it is as though her heart stopped. Two other symptoms—long continued irritability of the bladder, and the other a giving way of the legs. On December 10, she found for a few days that her knees suddenly and without warning gave way on her coming down stairs. In October she complained of the same coming on in the morning, and passing off in the afternoon."

November 28, 1900: Still troubled with perspirations. Tachycardia continues. She has some looseness of the bowels, but is gradually improving. Has marked tremor of the eyelids on closing.

REMARKS.—This history suggests the question: Did this patient need to have goitre and exophthalmos also to become then —and not till then—a case of Graves' Disease?

CASE XXIII.—Mrs. A. S. Æt. 37.

Tachycardia. Gastro-intestinal derangements for two years. Nervousness. Headaches. General tremors. Tremor of the right hand and of eyelids. Weakness of the knees. Loss of hair. Pains, marked, in the heels. Tinnitus. Worse mornings.

November 17, 1900: Referred to me by Dr. D. E. Walker, of this city, as a case of rheumatism of the right heel and instep, supposed to be due to painting of her room. I found that she had the symptoms of persistent tachycardia—pulse ranging between 130 and 140. Says she had great trouble with her stomach for two years, frequent nausea, with occasional diarrhœa; frequent migrainous headaches; muscæ volitantes; general tremors, especially of the right hand; marked weakness of the knees; great tremor of the eyelids; always worse in the mornings. For the year past she has marked falling out of the hair;

is extremely nervous, and has shifting pains in different parts of the body. No migrainous history in her family. No pains in the ears, but very annoying tinnitus in both ears. Much troubled with bad dreams. No sign of enlargement of the thyroid; no exophthalmos; and no eye symptoms.

REMARKS.—This patient furnished another illustration of the presence of Graves' Disease not being recognized, simply because she did not have exophthalmic goitre; and instead was referred to me because the supposed rheumatism in her heels would not yield to anti-rheumatic remedies.

CASE XXIII.—Miss L. S. Æt. 24.

Tachycardia. Chronic gastric symptoms, with intractable diarrhœa. Nervousness. General tremors. General weakness. Weakness of knees. Headaches. Pains in ears, neck, finger tips, heels and toes. Worse mornings.

January 25, 1901: Sent by Dr. H. S. Houghton, of this city. She has been a chronic dyspeptic, with frequent nausea and constipation. For a year and a half she had diarrhœa, which is uncontrolled by medicines. This patient always feels worse in the mornings. Eyelids tremble. She has much flatulence; also great weakness of the knees; very frequent headaches; mucæ volitantes often like stars; frequent pains in the ears, with post auricular pains, more on the left side; pains in the fingers, toes and feet. No insomnia; no irritability of the bladder; no itching. Migraine not in her family, except one out of several sisters. Pulse 124. April 2: Comes asserting that she is still the same—in her pains, and in her tremors; and now has pains in the heels, down her neck and in the ears. Pulse 110.

CASE XXIV.—Mr. F. W. Æt. 43. Morristown, N. J.

Tachycardia, of long standing. Gastric derangement. Tremor of right hand. Weakness of the knees. Vesical irritability. Itching. Worse mornings.

December 20, 1899: He is much troubled with tachycardia, especially after eating, but says that walking and exercise do not increase his palpitation. Also says that he has had it for eight years, along with a great deal of gastric dyspepsia. He is much troubled with constipation. No valvular trouble. Pulse 120.

January 3, 1900: Some improvement. Pulse 102. February 13: Improved; says that he wakes in the morning with a sense of heaviness at the stomach. Lids tremble

on closing. Occasionally has annoying tremor of the right hand, and also a pronounced weakness of the knees. He has considerable irritability of the bladder; and sometimes itching without eruption. Pulse 100. The only pains he complains of refer to the cardiac region.

1903. This patient has quite recovered his health, with improved digestion and a normal pulse.

REMARKS.—This patient claimed that he had long been under treatment for his stomach, without any benefit, until put on treatment for Graves' Disease.

CASE XXV.—Mrs. B. Æt. 33.

Tachycardia. Great prostration. Gastric flatulence. Nervousness. Tinnitus. Tremors, including right hand. Headaches. Vertigo. Weakness of knees. Pains in heels. Paræsthesiæ. Insomnia. Itching. Vesical irritability. Worse mornings.

October 1, 1901: I was called to see her for supposed heart trouble, by her physician, Dr. Moser, of this city. I found an extremely rapid action of the heart, but no other signs of cardiac disease. Pulse 160. With sensations of fainting; great general weakness and prostration. Patient is very well nourished. She had an attack of this kind five years ago, which confined her to her bed for several weeks. She is greatly troubled with flatulence; with a ringing in her ears; and with shifting pains in different parts of her body. Denies being a chronic dyspeptic before. Has constant insomnia; considerable vesical irritability; itching in different parts of the body, most in the ears. Also paræsthesiæ, numbness in both hands and in the feet; constant severe headaches. November 30: She comes to my office with the statement that she was greatly improved in all her symptoms, till after five weeks' treatment she took some green peas with cold roast chicken, and had violent pains set in in her head. Ever since that she has had a stuffy feeling in her ears; increased nervousness and bad dreams. Eyelids very tremulous; tremor of the right hand, with weakness of the knees so pronounced that she dare not go around alone. December 7: Greatly improved. Pulse only 78. Has had but one attack of dyspepsia. December 26: On the 21st she had a prolonged chill in the night, and ever since then has had gastric distress, a great ringing in her ears, and is very nervous. Pulse 110.

January 9, 1902: Got along very well, but lately has had a return of the distress in the head. February 20: On the whole better; but is troubled with a sense of vertigo on waking in the

morning. Always feels worse in the morning. March 7: Has had attacks of the heart sensations at night, in which she feels dead. This is followed by palpitation, much tinnitus in the left ear, and a sense of inward tremor. Pulse 100. Has occasional chills in the morning on first waking. March 22: Nervous and apprehensive; bad feeling in her eyes; a good deal of vertex headaches. The tinnitus is more in the right ear now. Pulse 100. Still has the inward tremor; tingling in the left hand and foot. But the greatest complaint now is of vertigo. April 14: Comes with all the typical symptoms now, and with pains in the heels. May 8: Was better for awhile, but lately has had much palpitation. Pulse 120. Occasional pains in the heels. June 10: On the whole better, but with a relapse. The palpitation and nervousness continue. No migraine in herself or family. Pulse 110. Less flatulence and less tinnitus. June 28: Feels a great deal better of all her symptoms. Pulse only 86.

REMARKS.—Among the more pronounced symptoms of this patient were the intense prostration, when the tachycardia went along with palpitation, and the fear of falling from the weakness of the knees. The relation of all her symptoms to the degree of her digestive derangements was very constant.

I originally included the histories of three other patients (women) in this list, one of whom has a sister with exophthalmic goitre, but I have decided to omit them on account of the preponderance in them of migrainous headaches with gastric derangements. They might, therefore, be classed by some as simply dyspeptics, with headaches and nervous symptoms common to neurasthenics, and not as cases of Graves' Disease. But persistent tachycardia, which was present in each of them for periods varying from one to two years in duration, is not a characteristic of migraine, but the reverse, for its symptoms are periodical and not continuous, while we must insist that such tachycardia links itself to no other than Graves' Disease.

Another fact about these patients is the continuousness also of their ill health, marked by muscular languor, depression and anæmia, without any days—or even hours—of buoyant vivacity and spirits which so many persons subject to simple migraine show in the intervals. Graves' Disease never ceases to be dismal as long as it lasts.

CASE XXVI.—Mrs. C. Æt. 48.

Tachycardia. Emaciation. Extremely nervous. Sense of constant inward tremor. Tremor of the right hand. Weakness of the knees. Cramps in calves of legs. Wandering rheumatoid pains. Recent loss of hair. Sweating. Itching. Vesical irritability. Much twitching of the eyelids. Tinnitus in left ear. Intestinal flatus. Always worse in the mornings. Severe occipital headaches. Various paræsthesiæ. Aphasia. Bulimia. Constipation.

April 28, 1903: For two months back this patient has been losing flesh, amounting to 13 lbs. Has been growing very nervous, quite unusual for her. Complains of a sense of constant inward tremor; affects her right hand so that she cannot write as well as before. Great weakness of the knees, so that she cannot walk now as she did two years ago. Has some cramps in the calves of her legs; wandering rheumatoid pains, particularly in the region of the heart. Has lately noticed that her hair comes out. Troubled with perspiration. Some itching of the skin. Some vesicle irritability. She has a good deal of trouble with twitching of the eyelids. Recently tinnitus has set in in the left ear. She has considerable intestinal flatus. Always worse in the mornings, when she has frequent occipital headaches. She has been a great meat eater; takes very few vegetables. Pulse 100.

May 29: Reports she is a great deal better in all her symptoms. Pulse 80. Left ear feels full.

July 18: Had been much better; but one day, after taking peas, she had a sense of indigestion. This was followed by a relapse of all her symptoms. Weakness of the knees; roaring in the left ear; various paræsthesiæ, and once had an attack of aphasia. She also is troubled with bulimia.

October 1: Patient writes to me that her condition is very much improved; better of cramps in the legs; bowels now move naturally, the first time in years. Tinnitus now only occasionally. Twitching in the eyelids gone.

CASE XXVII.—Miss S. Æt. 50.

Tachycardia for sixteen years. Great nervousness. General tremors. General weakness. Weakness of knees. Abasia. Aphasia. Mental depression. Occasional mania. Aggravated tinnitus. Pains in neck. Persistent gastro-intestinal disorders. Great emaciation. Insomnia. Pigmentation. Vesical irritability. Worse mornings.

Seen in consultation with Dr. H. W. Mooney, of this city, December, 1903. Eight years ago she was pronounced to be a case of Graves' Disease without goitre by Dr. R. Van Santvoord,

who then treated her. I found her very much emaciated and scarcely able to stand. Pulse 140. Tremor very marked, at first in right hand, now general. Her chief complaints are of excessive nervousness with great weakness, especially of the knees, so that she has had frequent falls. Through all these years she has been a constant sufferer from gastric and intestinal flatus with intervals of diarrhœa. Her chief complaint is a distracting tinnitus which seems at times to make her delirious. At other times she is very willful and unreasonable. At times she has temporary aphasia. Complains of no pains except in the left side of the neck. She is very insomnic, has frequent vesical irritability and is always worse in the mornings. She never had any enlargement of the thyroid nor exopthalmos.

SUMMARY.

The justification for adding another to the long list of publications on Graves' Disease—in Kocher's Bibliography amounting already to over 1400—is to be found chiefly in the records of my cases, which indicate that this malady may develop and run its course, even to a fatal issue, without any recognizable connection with the thyroid gland. In every one of these patients the condition of the thyroid gland was examined carefully and repeatedly for signs of undue fulness of its blood vessels, as well as for any indication of enlargement of the gland itself. The thyroid is surely not a difficult organ for either inspection or palpation, as it is hid in no cavity, and is easier to examine than the mammary gland itself. In Case V it seemed to be atrophied, as it often is in women of her age, and the same may be said of Case XI. The only criticism that can be urged is that the history of some of these patients, particularly of some of the consultation cases, was of too recent date, and that the goitre might appear in them later. But I might have had to wait for ten years to elapse before I could be sure on that point. As it stands, more than two-thirds of the number have been under my own observation for periods varying from two to twelve years. If these histories, therefore, suggest that the implication of the thyroid gland bears only a secondary, instead of a primary, relation to Graves' Disease, we may then be led to look elsewhere for the *causa causans* of this malady, with a corresponding modification in the indications for treatment.

Hence, the evidence that would support the foregoing statement should be scrutinized carefully; and it is on that account that I prefaced the histories of the 28 patients, in whom at no time was there any palpable evidence of affection of the thyroid or of eye change, by the clinical details of the 42 patients who did have Graves' Disease with exophthalmic goitre, in order to

show that just the same peculiar symptom complex was present in both sets. This evidence, based upon a detailed comparison of clinical details, seems to me conclusive, because with proper attention there can be no mistaking a true case of Graves' Disease, not only because of the number and variety of its special symptoms, but still more on account of the peculiar relation of the symptoms to each other. This fact is quite analogous to the certainty of identification of substances in spectrum analysis which, as in the eighty principal lines in the spectrum of iron, are conclusive not because they are eighty lines, but because they are grouped in such ways as to render practically *nil* any chance of error.

To begin with, there is much significance in the fact that many and diverse though the symptoms be, yet they have a family resemblance, so to speak, in common, and which as such is invariable. Thus, whatever functions or organs be implicated, there is never an inflammatory element present from first to last, however severe or prolonged the disturbance. No organ in Graves' Disease, including the thyroid itself, is ever inflamed. The tachycardia, for example, of Graves' Disease (as we have already pointed out) is unlike any other tachycardia in its long duration and in its independence of any other cause of rapid heart action. Its remarkable persistence is matched only by its invariable lack of association with any other cardiac disorder, coupled with as constant an association with the varied derangements of wholly other organs as they occur in Graves' Disease. We may, therefore, rate this tachycardia as truly specific, so that when it is this form which is shown to be present, by the exclusion of every different cause of hurried heart action, the conclusion becomes certain that none other than Graves' Disease can be the cause, whether goitre be there or not. This specific tachycardia was present in 27 out of 28 of the patients without exophthalmic goitre throughout the whole time they were under observation until the disease itself subsided, and the records of its duration include such periods as from two to nine years.

Again, the symptoms of Graves' Disease always show certain peculiarities, even when they resemble the symptoms of other diseases. Thus, the different affections of the special sense organs are so unlike disorders of these same organs in other conditions,

that they constitute of themselves a proof that they also are specific. In the case of the aural derangements, for example, the tinnitus may be more continuous and distressing than any tinnitus due to an organic lesion. In time, the diminution of hearing may progress until, in one ear at least, the deafness becomes total. But all the while not a sign of any local process in any of the aural structures can be detected. There may be pain, but it is not where pain in ear disease is oftenest located, and usually it consists only of superficial tenderness of the auricles or of adjacent parts of the neck. But the most convincing evidence that the ear affection is due solely to the cause of Graves' Disease itself, and is not at all a complication, like an intercurrent otitis media, is shown by its complete subsidence when Graves' Disease itself subsides. The local tenderness, the tinnitus and the deafness all get well together, because the patient has recovered not so much from them as from some twenty-six other disturbances besides—in other words, from Graves' Disease. But as our histories show, the patients without exophthalmic goitre had exactly the same ear troubles, both in ratio and in kind, with those who did have goitre.

No less complete is the parallel in the case of the motor symptoms. The tremor of Graves' Disease is wholly of its own kind in resembling the physiological tremor of fright only, and not the tremor of any recognized organic form of nervous disease. It is peculiar also in the parts which are involved, and in the fashion in which they are affected. No other affection persists for days together shaking the right hand only in the morning. In no other disease are the knees so separately weak. While every case of abasia in Graves' Disease is a pure stumble, from which the patients rise as quickly as any others from an accidental fall. As previously detailed, six of my 42 goitrous cases could not write in the morning, but could do so in the afternoon; while the same is recorded of three of the 28 non-goitrous cases. While as to abasia, four of the non-goitrous cases had just the same falls as 8 of those with goitre.

Equally conclusive are the peculiar features of the derangements of the alimentary canal. In the histories of the 42 patients with goitre, both the gastric and the intestinal disorders were

marked by the same unvarying symptoms through months, or even years, never assuming inflammatory characters, or inducing organic changes in either stomach or bowels, even when in the fatal cases they appear to have been the chief cause of the patients' death. But so were these derangements identically the same in every particular among those who never had a sign of thyroid disease. With all their chronic gastric distress and flatulence, there was never a sign of gastritis; and the persistent diarrhœa never changed into an enteritis or a colitis. Likewise, the numerous and peculiarly located pains in widely separated parts of the body were among both classes equally devoid of all evidences of neuritis. Similarly with the rest of the list of derangements. Both classes showed equally in the ratio of irritability of the urinary bladder, with the same absence of signs of cystitis, and of annoying pruritris without even erythema. While in the particulars of emaciation, loss of hair, sweating, bulimia, etc., the patients without goitre showed in every one of them a like proportion with those who had goitre.

Finally, there are two correspondences which of themselves seem decisive. The first of these is that in the great majority of instances Graves' Disease is no transient or changeable derangement; but, on the contrary, a chronic complaint causing a prolonged invalidism, which affords ample opportunity and time to arrive at a certain diagnosis. Because through it all the malady remains the same, not losing its individuality, nor merging into anything else, while its particular symptoms retain unchanged their own characteristics. Diabetes mellitus itself could not be more special or continuous in its clinical course or accompaniments. But, as the records show, the stories of my patients without goitre lacked nothing of that continuous sameness of Graves' Disease which proves its distinct and specific nature, as it may progress, but never alter, however chronic its course.

We need only cite, as a conclusive illustration of this fact, the histories of the two sisters, Case II (*a*) of those with goitre and Case I (*b*) of those without goitre.

Case II (*a*) was for three years severely affected with tachycardia, nervousness, local and general tremors, including tremor of the tongue, distressing tinnitus, pains in the eyes, headaches,

mental depression, vertigo, general weakness, weakness of the knees, peculiar pains in different parts, paræsthesiæ, obstinate gastric distress, occasional diarrhœa, insomnia, sweating, etc., and finally after three years she developed goitre as she was getting well. If her disease was due primarily to derangement of the thyroid gland, that organ showed no signs until at the last it rather suddenly hypertrophied with apparently a beneficial effect, for soon afterwards all the various troubles of the patient subsided, and ere long the belated goitre disappeared also.

Meantime her sister, Case I (*b*) without goitre, slowly developed a tachycardia lasting nine years, during which she had frequent nausea, gastric flatulence, occasional diarrhœa, tremor, both general and in the hands and tongue, weakness of the knees, tinnitus, pains in her left ear, with sensitiveness to touch, local pains in the right clavicle, in the shoulder, left side of the neck, in the finger tips and heels, alternating blindness in the right and left eye, vertigo, paræsthesiæ, itching and vesical irritability. But at no time during her prolonged trouble has she shown any more signs about her eyes or thyroid than her sister did for three years before her goitre developed, and it is not at all likely that she ever will have exophthalmic goitre, for during the year 1902 she has recovered from all her symptoms, the last to cease permanently being the tachycardia. Now, no physician who could have attended these two sisters throughout their illness would doubt for a moment that both had the same disease; and, as already stated, both these patients firmly believed that their mother died of the same complaint, though she never developed goitre.

Another close correspondence between the two classes is found in the exact parallelism of the whole story to the very end, when the end is death, as is fully illustrated in the accompanying particulars of two fatal cases who had goitre, and of two who never showed signs of thyroid enlargement. But when any disease continues progressing for month after month, unchanging its course, to end at last in death, it is useless to pronounce it an undeveloped, or an abortive, or a latent form of any disease, merely because a symptom common with other examples of that disease is absent.

Moreover, the demonstration of the independence of Graves' Disease of thyroid gland disease, is practically important, in my opinion, on account of its facilitating a correct diagnosis of many cases of ill health, the true nature of which is often not suspected. With a disease as definite in its pathology, and we may add, in its treatment, as diabetes mellitus, these patients are rated instead as hysterical, or neuralgic, or neurasthenic, or rheumatic, or dyspeptic persons; or, as I have known, they have been pronounced to be tuberculous, or affected with heart disease, or with kidney disease, or with brain tumor, or with cancer of the stomach. With others, their physicians have confessed to me that they were wholly unable to make any diagnosis, which they could have readily done had they thought that Graves' Disease might occur without exophthalmic goitre. But one special advantage of such a demonstration would be the recognition and proper treatment of that numerous class who have Graves' Disease only in an incipient or mild form. Obstinate dyspeptic symptoms, with headaches, neuralgias and nervousness, may all be found to fall into a consistent relationship to one definite malady, when once the clue is discovered by an accompanying persistent tachycardia. Such patients can often be soon relieved by special treatment at the beginning, when, if allowed to continue, they become as settled in their derangements as in any other chronic specific malady.

Finally, there is one consideration which, to me at least, is fully confirmatory of the positions taken, and that is that the various measures, both dietetic and medicinal, which are found to be most effective in relieving patients with Exophthalmic Goitre are equally advantageous to this class without goitre. As will be explained, this system of treatment is specific in the sense of not being directed against the symptoms of the malady at all, but against their supposed cause, and, therefore, could not be beneficial to both classes alike unless they shared equally in that cause.

FATAL CASES WITH GOITRE.

CASE I.—Mrs. M. Æt. 51.

October, 1880. First consulted me.

I had known her well for some time from having attended other members of her family. But she had always been healthy before, so that I had not seen her for some months. I was much struck by the change from her former appearance by so many signs of emaciation; and she began her story in a hesitating manner, as if she were about to divulge some cause of mental distress. Her voice trembled as if choked with emotion, her hands trembled, and her respiration was hurried and catching. She said, however, that she had had nothing to make her so nervous, nor could she imagine why she was so. She supposed that her nervousness also caused her to be very insomnic. Meantime she had had diarrhœa all summer; but other people had diarrhœa without being as nervous as she was. As soon as I examined her pulse and found that it was over 140, while her temperature was normal, and as I noticed the extensive muscular tremor, I felt assured that she had Graves' Disease, though careful observation showed no sign then of either enlargement of the thyroid or exophthalmos. As at that time I had not been led to devise the form of treatment of Graves' Disease which I have subsequently adopted, I tried for a number of months the administration of belladonna, the bromides, digitalis, silver nitrate, iron, arsenic and the iodides in succession, without satisfactory results. The diarrhœa continued for many months, unchecked by astringents; and, at last, more than a year after the beginning of her illness. the right lobe of the thyroid became enlarged. Exophthalmos, however, never developed up to the date of her death, three years after the commencement of the disease. As the patient, by the time the goitre first showed itself, was confined to her bed by her weakness and tremor, I recommended a complete change of diet, and directed that she should be fed exclusively with "matzoon," or fermented milk and stale bread. The change for the better upon this diet was surprisingly rapid and progressive. The diarrhœa stopped without medicine, both her nervousness and sleeplessness improved, and finally the pulse became remarkably lessened, down to 80-90. In two months she seemed con-

valescing, and was able to go about without fatigue. Four months afterwards, contrary to my advice, as she felt quite well she discontinued the matzoon, and resumed a meat diet, of which she was always very fond. Upon this she went out in the country, and on returning (after two months' absence) I found that all her symptoms had recurred, including the diarrhœa. She again was put on matzoon, and again she improved. And this time she continued the milk for about six months, with such a gain in flesh and strength that she declared herself quite well. She then ceased consulting me—as I afterward learned—from fear of my insisting on the milk diet—until after nine months I was called to see her, and found her worse than ever, because of the addition of mental symptoms of irritability and obstinacy in refusing all treatment, with occasional attacks of delirium. She declared that she would rather die than take matzoon, and nothing would persuade her to take milk in any form.

One day I was sent for, to see her, because she seemed so low. I could scarcely count her rapid pulse; and while I was again trying to do so, it suddenly stopped, her pupils dilated, and the patient was dead, with scarcely a perceptible struggle. . .

CASE II.—Mrs. C. Æt. 27. Patient of Dr. Carrie L. Black, who kindly furnished the following notes of her illness:

August 1, 1890: First consulted Dr. B., stating that her stomach had been irritable, and that she was greatly inclined to nausea, which was extremely persistent. She was also liable to frequent attacks of migraine, often so severe as to confine her to her bed for two or three days. During these attacks of indigestion, her tongue was red, clean and moist. She also had an obstinate itching, which was only relieved by a change of climate. She was greatly troubled with constipation. Pulse rapid, rarely below 90, and then becoming extremely irregular, reaching from 120 to 140 per minute. She also had at that time a slight enlargement of the thyroid.

During the following year she was subject to bronchitis, with asthmatic breathing. Being a society woman, she could not be persuaded to rest from its excitements, which were often followed by attacks of extreme prostration and headaches.

In 1895 she complained frequently of attacks of dyspnœa and palpitation, at which time the thyroid was observed to augment perceptibly.

Twelve months later, in 1896, it was noticed that her eyes protruded somewhat.

Following upon distressing family misfortune in the spring of 1898, her dyspnœa and palpitation were very much increased,

the pulse varying from 130 to 150. She became excessively nervous, with a good deal of gastric disturbance. She had also become very much emaciated.

On September 10, 1898, she had a severe attack of diarrhœa, accompanied by muscular pains over the body. On the night of the 20th, she had a chill, accompanied by nausea and vomiting. She was accustomed to have these nocturnal chills at that time. She complained bitterly of muscular pains, especially about the right shoulder and chest, and some aching also in the lower limbs. Her pulse had fallen to 72, and was very irregular. She had great nausea, with retching and vomiting, which greatly exhausted her. This patient had had a peculiar bronzed appearance for some years before, but this had disappeared. On September 26, her pulse was 132, temperature 102½°. At no period, until a few hours before her death, did the temperature fall. The nausea continued, and was only relieved by single drop doses of Fowler's Solution.

Shortly after Dr. Thomson's call, she had a rectal hemorrhage, followed almost simultaneously by signs of a cerebral hemorrhage. Her speech became thick and indistinct, and hemiplegia of the limbs on the left and the facial muscles on the right, with ptosis of the right lid, supervened. She remained unconscious for some 20 minutes, with every indication of impending dissolution. After various stimulants were employed, within an hour the patient rallied sufficiently to express herself interested in the efforts made for her recovery, commenting upon the consultants, etc. The patient now became excessively restless, excited and delirious, while the signs of hemiplegia decreased. About two hours before she finally sank, she became more conscious of her condition, and conversed for some time. The heart then failed to respond to any stimulants, and the patient finally expired, without a struggle, at 3.15 P. M., on September 27, 1898.

Examinations of the urine were made by microscope and chemical tests, not only during this last illness, but often previously, with no signs of kidney disease, or of the presence of sugar. The patient had, however, for over two years been greatly troubled with irritability of the bladder, as well as by insomnia.

FATAL CASES WITHOUT GOITRE.

CASE I.—Mrs. P. Æt. 44. Clifton Springs, N. Y.
November 30, 1893. Family history:

She has a brother who is suffering from Addison's Disease. She has been a patient of Dr. Wm. H. Phelps, of Lyons, N. Y. She has been feeling very debilitated, so weak that she could scarcely get about all summer long; extremely nervous, with a constant tendency to diarrhœa, and weakness of the knees, so that she would fall if she stood up; rapid emaciation. She then came to the city to consult a Homœopathic physician, who said he found a considerable quantity of albumen in her urine. He announced to her friends that she had heart disease. He then became puzzled by the albumen totally disappearing. The specimen brought to me showed a specific gravity of 1020; natural color; no albumen or casts. I was called in to-day, and found her in bed, unable to walk from weakness. Pulse 140. Pronounced throbbing of the carotids and femorals; no evidence whatever of goitre or exophthalmos; constant diarrhœa; normal temperature. Said she had been losing flesh steadily, and was now losing her hair.

December 2: Mrs. P. has had uncontrolable greenish vomiting all day, with persistent diarrhœa. December 3: Slightly better. December 4: Worse this afternoon, with nausea, though less vomiting. Pulse became extremely rapid and intermittent. The family states that she had a sinking spell in the afternoon. December 5: The vomiting continues and the diarrhœa. December 7: She has become extraordinarily restless with her feet, so that she has bruised her ankles, and is often delirious. Pulse 120. Has been more quiet, vomiting not so often; diarrhœa less. December 9: Found her pulse extremely irregular. She would insist on getting up to have a passage of urine or of the bowels, and each time the nurse noted that she became more nauseated. December 10, 3 P. M.: She was maniacal most of the forenoon, insisting on getting out of bed. This afternoon, after doing so, she suddenly fainted, and died without a struggle.

The most embarrassing feature of this case was the intractable vomiting and purging. The vomited matters were green liquids,

and her breath had a strong, sweetish acid odor. At no time was there any sugar in her urine. After her death I received a letter from her physician, Dr. Phelps, in which he stated he could make no diagnosis of Mrs. P.'s case, except that she was in all respects similar to the case of his own wife, who died a year before with the same symptoms.

CASE II.—Mrs. C. S. H. Æt. 68.

This case is the sequel of the remarkable history of Case V, who had such a very serious illness, but seemed to have recovered, as therein detailed.

May 13, 1901: Within the past two months this former patient of mine showed symptoms of a relapse. I was called to see her on this date at their suburban home, and found her suffering from serious symptoms of cardiac weakness, orthopnœa, with attacks of suffocation. Some edema of the feet, and inability to sleep from dread of suffocation. Pulse 130, very weak and irregular. May 15: Much troubled with nausea and flatulence, but otherwise improved; some pains in her ears; some diarrhœa to-day; very nervous at night. May 18: Sleep better. Sometimes paraphasia, of which she is conscious and much annoyed by it. May 24: Edœma rather increased. Her mouth sore again. Her sleep not so good. May 27: Had two attacks of vertigo, after one of which she did not know where she was. Tongue red and raw. Pulse intermittent. May 29: Symptoms of cardiac weakness on exertion increasing. June 3: Has not been doing well. Greatly distressed with flatulence. Find it difficult to get her to take milk. June 11: Greatly relieved of her flatulence by drop doses of Fowler's Solution every hour, so that she passed a better night than for weeks. June 12: General symptoms improved, especially her pulse and breathing; but she wanders a good deal, and at times does not know where she is. June 14: Pulse steady to-day and strong, 102. No dyspnœa; no edœma of the feet; tongue very red and glazed. June 17: Improved in all respects, except some diarrhœa. June 19: Sleeps better. Improving in her breathing. June 24: For two nights has not slept so well. Has some cardiac symptoms again. July 1: Fairly comfortable. July 5: Some nausea and intermittent pulse. After my call this afternoon a violent thunder storm came on, at which, as usual, she was much frightened and had increased nausea. After swallowing some hot water, she said she felt relieved. She then got up, walked into the adjoining room, sat down and leaned her head against the bed, and soon was dead without a struggle.

PATHOLOGY.

In discussing the pathology of Graves' Disease, the commonly accepted view that it is due to a specific disorder of the thyroid gland merits the first consideration. As in the case of derangements of other glands, we should begin first with what is known of the physiological functions of the thyroid itself, so far as these have been determined. At first sight it would seem as if we would have no lack of material for this purpose, for there is no organ of the body whose normal relations to the economy have been so assiduously studied, until in fact the literature growing out of experimental researches on this subject has become quite unmanageable in bulk. Instead of final conclusions, however, some new factors in the problem continue to be reported from time to time, which more or less considerably modify all previous inferences. Therefore, with the physiology of the thyroid in such a state of uncertainty, we are in no position to dogmatize on its pathology.

After years of experimentation on animals of the effects of depriving the system of the thyroid secretion, by excision of the gland, it was inferred that in carnivora this operation was rapidly fatal, in omnivora less so, and in herbivora scarcely at all. Thus, in dogs it was soon followed by tremors, then by fatal tetanic spasms and convulsions. Horsley found that monkeys survive the removal of the thyroid much longer than dogs, and if kept warm they develop a condition similar to myxedema in man. With herbivora they seemed generally to get along quite well without the thyroids; a curious illustration of which is shown by a recent treatment of Graves' Disease recommended by Lanz, Möbius and other writers by large quantities of the milk of goats which have been thyroidectomized. Thus it appeared that the effects of removal of the thyroid differed materially, according to the normal diet of the animals experimented upon.

But more recently the whole subject has been given another turn by researches on the functions of the small bodies named the parathyroids. In some animals, these are embedded in the thyroid glands, somewhat like the islands of Langerhans in the pancreas, so that they are removed along with the thyroid when it is excised. It is this fact which has led to the confusion in the interpretation of the symptoms following this operation. In other animals they are quite separate, or separable, from the thyroid, and as this is the case in rabbits, Gley was able to explain why thyroidectomy seemed to cause so little effect in rabbits, for on removing the parathyroids alone in them the full train of nervous symptoms developed, even though the thyroid was left intact. Gley was first inclined to regard the parathyroids as capable of compensating for the thyroid tissue when this is removed, but that view is now generally abandoned, and as MacCallum[1] states, "there is no histological proof that parathyroid tissue can ever become converted into thyroid tissue, and there is now a general agreement of opinion that these glands are organs of very different nature."

What, therefore, the specific function of the parathyroids is has been recently investigated by numerous experimenters. That there is a virulent poison, which reaches the nervous system through the blood when the parathyroids are removed, and which does not act in health because it is neutralized in the parathyroid cells, or by their secretion, is indicated by the fact that in dogs the fatal tetany, rapid breathing, etc., are immediately ameliorated by bleeding the animal freely, and injecting an equivalent amount of normal saline. The poison then accumulates for 24 hours and the tetany, etc., returns, to be again relieved as before by the same procedures, showing that they wash the poison out. The further question then, where in the body this poison is generated, whether absorbed from the intestine, or formed in muscle or nerve metabolism, cannot yet be decisively stated, but in favor of its food origin are the reports of Verstræten and Vanderlinden, that the tetany is less violent and appears later when the dogs are kept on milk, than when

[1]W. G. MacCallum, Transactions Am. Assoc. Physicians, vol. xviii., p. 35, N. Y. Med. News, Oct. 31, 1903.

given a pure meat diet; and in confirmation, MacCallum fed a parathyroidectomized dog exclusively on bread and water after the operation, and in this case no tetany developed within the twenty days that the dog lived. Numerous experimenters have also stopped, or delayed, the development of the nervous derangements by giving emulsions of the parathyroid glands themselves.

These conclusions cannot fail materially to affect the problems connected with the pathology of Graves' Disease. Now, that the thyroid is proved to be a compound organ, as much so as the pancreas, one theory, that of excessive thyroid secretion, will have to be readjusted, and the respective shares of the functionally different structures connected with the thyroid need to be analyzed.

As far, therefore, as they can be separated, we may say that it looks as if the chief function of the thyroid itself was connected with general metabolism, and that deprivation of its secretion, by thyroidectomy alone, leads to the more chronic symptoms characteristic of myxedema, while removal of the parathyroids alone leads to acute intoxication, with nervous symptoms. Does increase, or decrease, of the secretion of either of these cause its corresponding manifestations in the symptoms of Graves' Disease? So far as the nervous symptoms of this disease are concerned, which correspond to what can be observed in animals experimented upon, such as muscular tremors and weakness, they point to deficiency of parathyroid secretion rather than to increase. But observations on the condition of the parathyroids in Graves' Disease are as yet too few to decide. In one fatal case of Graves' Disease, MacCallum reports that no trace of parathyroid tissue could be found at autopsy. In eight other cases, where one lobe of the thyroid had been removed by operation, in two no definite change could be made out except diminution in size; while in two distinct degenerative changes in the parenchyma cells were found; and the parathyroids were distinctly smaller than normal in all. As far, therefore, as the parathyroids are concerned, it would seem that diminution or absence of their secretion, rather than hypersecretion, is the most probable condition in Graves' Disease.

On the other hand, to consider the thyroid separately, we are enabled in human pathology to study examples of isolated affections of this gland in the sense that it and no other organ seems to be involved in the morbid process. While adenomatous, cystic and malignant tumors occasionally develop in its substance, it does not differ in this respect from other glandular structures. But it is quite otherwise with parenchymatous goitre, because it can be accounted for only on the supposition of some abnormal stimulus acting upon the organ, with hypersecretion and consequent hypertrophy as the result.

Nor could be ask for a more complete example than in this very common affection of a distinct diseased condition of the thyroid with definite characters in its anatomical changes, and with definite factors in its causation. A more localized affection is not to be found, and hence, one which might be expected to illustrate the functions of the organ by showing how they are interrupted or modified by such marked organic changes. The fact, however, is that instead of doing any such thing, its tumor might as well be a lipoma in the necks of the majority of these patients, which causes symptoms only by its mechanical pressure on adjacent parts. Otherwise, not a single separate constitutional disturbance, equivalent to any one of the twenty-eight symptoms of Graves' Disease, which we have enumerated above, accompanies this purely thyroid disease. This fact is commonly ignored by those who ascribe the long array of the constitutional derangements of Graves' Disease to a secretory activity of this organ, for why cannot a gland which is stimulated even to overgrowth in parenchymatous goitre, do *something* like the Graves' goitre, even if it be only sweating or vesical irritability?

When we turn to facts relating to the etiology of parenchymatous goitre, the divergence of this purely thyroid affection from all relationship to Graves' Disease becomes still plainer. Parenchymatous goitre seems to have more connection with drinking water than with anything else, and hence is both endemic and epidemic. Instead of attacking seven women to one man, as in Graves' goitre, it affects both sexes alike, or exclusively members of the male sex on account of their circumstances, as in the case

of regiments in barracks, or boys in a boarding school. St. Leger[1] relates that the youths in a certain township in France, in order to escape military service, drank copiously from a well noted for causing goitre. Their thyroid glands rapidly enlarged, so that by this means they escaped military service. Lombroso relates a similar case in Lombardy, where the men made themselves goitrous in 15 days.[2] The water from such goitrous wells will cause also the thyroids of domestic animals, as horses and dogs, to enlarge.

Now, in the first stages of parenchymatous goitre there must be something which excites the gland to great activity. But we nowhere read, even in those instances where the goitre has been intentionally and rapidly induced by drinking from goitrous wells, when, therefore, we should presume that strong stimulus to secretion must occur, that the symptoms of Graves' Disease develop during the process. Prof. Adami[3] advances the surmise that the hypersecretion in parenchymatous goitre tends to stuff the gland cells so fully, that the secretion is thereby prevented from escaping into the circulation, but that in the nodular forms of such goitres some of it occasionally escapes into the blood stream, and thus accounts for a few cases characterized by paroxysmal tachycardia. I cannot regard this as anything but pure hypothesis, which is negatived by the total absence of Graves' symptoms in the history of the great majority of these patients from the very beginning, as well as at the stage of complete infiltration. How does it come about that none of this increased secretion escapes into the circulation before it finally engorges the cells?

Nor can it be said that the anatomical changes found in the secreting structures of this gland in Graves' Disease show any specific characters different from those in parenchymatous goitre, to which, therefore, we can ascribe the great contrasts between the two thyroid affections. Joffroy and Acard[4] give the results of six autopsies of patients dying from Graves' Disease, and

[1]Etudes sur les causes du Cretinism et Goitre Endemic.
[2]London Lancet, Aug. 15, 1903.
[3]Practitioner, Jan., 1901.
[4]Archives de Médaline experimentale. Paris, Nov., 1893.

according to them, no clear line of distinction could be found in the gland from the conditions in simple bronchocele. Vandervelde and Le Bœuf[1], from their examinations of the thyroid, in four autopsies, emphatically reject the theory of increased thyroid activity in Graves' Disease, stating that the thyroid in their cases resembled anatomically ordinary goitres. Prof. Greenfield[2] finds great hyperplasia of the secreting structure, and argues that this proliferation suggests increase of secretion, which it does, as it occurs also in the hypertrophied gland tissues of parenchymatous goitre with just the same appearances.

All that can be said, therefore, as regards enlargement of the thyroid is that quite different causes may induce it. It is an organ, which, like the spleen, seems to be very susceptible to toxic agents, acting upon it through the circulation. But this fact by itself fails to throw any light upon the pathology of Graves' Disease, because it affords no explanation whatever of the remarkable difference between the clinical symptoms accompanying a simple parenchymatous goitre and those accompanying an exophthalmic, for, as before remarked, no two diseases can be named so unlike in their systemic effects as these two goitres. So far, therefore, the most probable inference seems to be that goitres, as such, are always the secondary results of toxins acting on the gland itself, and that the great difference in the constitutional symptoms of exophthalmic goitre is due to a universally acting blood poison generated, just as in parenchymatous goitre itself, elsewhere than in the thyroid, but which involves this gland only as many other organs are also affected.

There is, however, another consideration which should be taken into account before estimating the share of the thyroid in the etiology of Graves' Disease. The effects of thyroidectomy vary, not only according to the habitual diet of animals, but also according to their age. Even in dogs, if they are old, thyroidectomy is neither fatal nor accompanied by the usual symptoms. In keeping with this fact, Kocher points out that post operative myxedema scarcely occurs at all in elderly people. Bourneville and Brecon put the limit of liability to post operative myxedema

[1]Journ. de Med. de Bruxelles, Mar. 3, 1894.
[2]Brit. Med. Journ., Dec. 9, 1893.

as early as the thirtieth year. Hale-White and others have shown that as age advances the thyroid degenerates, and in old subjects the normal glandular structure can with difficulty be recognized. These facts would imply that the function of this gland ceases in time to be necessary to life, and therefore, it belongs to the class of temporary and non-persistent organs, like the thymus, whose function, though essential for a time, yet becomes no longer so after certain stages of growth have been completed. The actual relations of such organs to nutrition are yet very obscure, but clinically Graves' Disease is met with after the sixty-fifth year, as in my Case V with goitre, and Case V without goitre, ending fatally in the last. In this patient the thyroid could scarcely be felt, and the same might be said of Case IX of Class II.

With the facts heretofore considered before us, we are now better prepared to deal with the theory that Graves' Disease is due to excessive thyroid secretion. Being a ductless gland, the quantity of its secretion, whether great or small, normal or excessive, must always be hypothetical. As to quantity, therefore, we have no means of proving or disproving what may be affirmed about it. So far this secretion has not been detected in the blood, because there are no known chemical tests for doing so, and as to clinical signs, we cannot be sure but that some of the symptoms, such as tremors, pareses, etc., alleged to be due to excess, may not be instead the effects of deficiency of thyroid, or at least of parathyroid secretion. Equally hypothetical must be any supposed variations in the quality of the secretions of this compound gland.

On examination, therefore, of the arguments advanced, this theory is found to be based almost wholly on two postulates. First: that the symptoms produced by large doses of thyroid extract, or of feeding with the glands themselves, are similar to some of the leading symptoms of Graves' Disease. Secondly: that the symptoms of myxedema, which are caused by want of thyroid secretion, are the opposite of the symptoms of Graves' Disease.

As to the first point, one would suppose from statements made in its support, that an artificial Graves Disease can be induced by the continuous administration of large doses of thyroid extract,

whereas it is only in a few particulars that the effects resemble the symptoms of this malady at all, while its most important and characteristic derangements do not follow the administration of thyroid extract in any doses. A feeling of giddiness, with cardiac palpitations and tachycardia, with some rise of temperature, are common after large doses, with an increase of excretion of urea and a loss of body fat, so that thyroid tablets have been prescribed against obesity. The tachycardia, however, is very moderate and temporary in its duration, while the other symptoms of the so-called thyroidism, instead of being peculiar to this substance, follow upon the administration of other animal extracts, particularly of the parotids.

On the other hand, the most characterisic symptoms of Graves' Disease, such as tremors, pareses, pains, pronounced digestive derangements, etc., are wholly absent. Having had myself considerable experience in prescribing thyroid extract for obesity, neurasthenia, melancholia, chronic skin diseases, and particularly to patients with deficient elimination of urea, I can testify that the symptoms produced by undue doses resemble much more the symptoms produced by the nitrites, than those of Graves' Disease. The tachycardia of thyroidism, for example, has nothing in common with that specific, unvarying and sustained cardiac overaction, which continues night and day, waking or sleeping, for hours, days, months and years, whether there be goitre present or not a sign of it.

As to the contrasts between the symptoms of myxedema and those of Graves' Disease, the fact that deficiency of secretion causes the one condition, by no means proves that symptoms of an opposite kind can be due only to excess of the same secretion. There may be causes fully capable of producing these symptoms quite other than thyroid hypersecretion; and that such is most probably the case follows from one important consideration, namely, that there is no other known example of specific disease due to hypersecretion on the part of any gland whatever. If this theory be true, then Graves' Disease stands alone in pathology. For in glands supplied with ducts, and whose secretions, therefore, we can investigate, every example of hyper-secretion, as in ptyalism, is always the result of some agent in the blood,

and not the result of the glands self excitation. Its deleterious effects are wholly due to drain; and, moreover, it is doubtful if there be any true permanent excess of its own normal secretions by any such gland or glands in the body. Why it should be different with the ductless thyroid, no one attempts to explain. In parenchymatous goitre, a blood poison is undoubtedly present which the thyroid had no share in producing, however much the gland is affected by it. Why is not Graves' goitre equally the effect of a blood poisoning the origin of which is fully as extraneous?

On the other hand, the objections to this theory are numerous and weighty. Thus, in the first place, the severity of the toxæmia in Graves' Disease bears no relation to the degree of thyroid hyperthrophy, if that be taken as an index of over-activity. The thyroid enlargement, when it occurs, is wholly unlike parenchymatous goitre in being very variable in every respect, increasing or diminishing, or even disappearing, with little or no correspondence to the general symptoms. This hypertrophy, instead of being a sign of the seriousness of the disease itself, as in the case of any other kind of tumor which infects the system, is practically one of the least important features of the malady. In practice, I pay no attention at all to the thyroid and never prescribe for its enlargement, expecting that to disappear of its own accord after treatment directed to wholly different functions.

In the second place, this theory fails altogether to account for the undoubted clinical fact that Graves' Disease may, and in truth frequently does, occur without any sign of implication of the thyroid gland, while the general toxæmia is as grave, and may be as fatal, as in any patients who have goitre. These cases, therefore, cannot be regarded as in any sense incomplete or abortive forms of this very specific malady.

Such examples of Graves' Disease without goitre strongly imply instead that implication of the thyroid is a secondary, and not a primary, element in the etiology of the affection. They seem to indicate that when thyroid hypertrophy does occur, it is due to over-stimulation of a normal function of the gland, most probably that of neutralizing certain blood poisons generated in digestion, this over-stimulation being caused by the ab-

normal quantity or quality of such poisons. On the other hand, the susceptibility of the thyroid to such poisons may vary in different individuals, or in the same individual at different times, as the spleen does in ague, causing much hypertrophy in some, moderate in others, and none at all in others.

Again, the theory of the thyroid origin of Graves' Disease affords no explanation of the greater liability of women to the complaint. In my list of the patients with goitre, there are thirty-six women to six men, and of those without goitre twenty-four women to four men, a ratio in keeping with other statistics of this disease. It is difficult to imagine why the thyroid itself should so differ between the sexes as to account for the preponderance of women. But it is quite otherwise, when we take into account the proneness of women to gastro-intestinal derangements in connection with menstruation, pregnancy and the menopause. In each of these conditions, digestive disorders frequently occur, with nervous accompaniments not unlike in nature to the incipient symptoms of Graves' Disease. In pregnancy a slight enlargement of the thyroid is very common, but equally so are the digestive derangements.

Lastly, I hold that the results of treatment based upon the gastro-intestinal origin of the toxæmia of Graves' Disease are so unmistakably superior to any measures, whether medicinal or surgical, devised on the theory of thyroid disease, that they confirm the inference which physiology itself suggests, that diet and digestion, and disorders connected therewith, are the chief factors in the etiology of Graves' Disease. Conclusions based on therapeutics need to be scrutinized carefully, but there is no reason why they should not constitute evidence when their testimony is uniform and consistent, as I think will appear in the following chapter on treatment.

There remain a few other theories on this subject which may be mentioned.

When nervous "irritation" was more commonly invoked than now as a source of specific disease, some organic changes in the sympathetic, especially in its cervical tracts, were suggested as causative of Graves' Disease. But as no corresponding anatomical changes could be uniformly demonstrated which would

point in this direction, this theory is generally abandoned. Much more, however, can be adduced in favor of localized lesions in the medulla. Filehne divided the anterior fourth of the restiform bodies and succeeded in producing exophthalmos, even after division of the sympathetic, with occasional enlargement of the thyroid. Other experimenters have produced similar results, especially of late Tedeschi,[1] who claims to have produced artificial Graves' Disease in dogs by lesions in the same region as Filehne, with the same effects in the general metabolism as in Graves' Disease, such as increased excretion of urea and of the urinary phosphates. After such lesions, the administration of thyroid glands much increases the symptoms, but if the thyroid is excised before the lesion in the restiform bodies, the symptoms are prevented. He concludes, therefore, that these lesions increase the vascularity and the secretion of the thyroid, and that partial removal of the thyroid is of service in neutralizing the effects of such hypersecretion. Of course, the criticism can now be made of these experiments that no precautions were taken to eliminate the share of the parathyroids in the results. That there may be a close association between the medulla and the thyroid is very probable, but that chronic irritation of a nervous tract will account for such a prolonged disorder as Graves' Disease is very unlikely, for as Fagge remarks, "It is a sufficient objection to any theory of the kind that a primary irritation of a nerve center, lasting for months or years unchanged, is yet unknown to pathology." On the other hand, there is nothing so distinctive of nerve poisons as their selective operation on special nervous tracts or centers, and the chief toxin in Graves' Disease, though it may originate in the intestine, may yet have as one of its properties to affect the restiform bodies in the medulla. MacCallum reports exophthalmos as an occasional result of parathyroidectomy, and as that, of course, is due to deficiency of secretion, it follows that the exophthalmos is caused by the unneutralized poison in the blood.

The mechanism of the exophthalmos is as yet wholly unexplained. Like the other symptoms of the complaint it is very variable in its incidence. In my forty-two cases who had goitre

[1]Jeorn. d. R. Acad. Med. di Torins, Mar., 1903.

it was present in 19, among whom it was but slight in five, present in one eye only in one, and in both eyes in one woman who had no goitre at all. It was absent in the remaining 22. This variability in the occurrence of exophthalmos in my list is in keeping with the observations of others. Thus, in Passlevi's series of fifty-eight patients at the Jena Polyklinic ten had no goitre, and thirty no exophthalmos.

Graves' Disease sometimes supervenes upon a previously existing parenchymatous goitre, of which my list contains two examples, Cases XXVI and XXXII. It is rather surprising that this does not occur oftener, for though there is no relationship between the poisons which affect the gland in these two conditions, yet it seems conceivable that the injury caused in the parenchymatous form would make the gland more vulnerable to the causes which induce the other. However, the rarity of the conjunction, even in localities where parenchymatous goitre is endemic, proves that there is no causative relationship between the two affections.

Glycosuria is an occasional epiphenomenon in Graves' Disease, but though some writers make a good deal of it, I would not assign to it an important relationship any more than I do to albuminuria.

TREATMENT.

There is scarcely any specific malady whose symptomatic treatment is more unsatisfactory than that of Graves' Disease. If the case be really severe, it will be found that the tachycardia is wholly uncontrollable by any the drugs usually prescribed for cardiac disorders, whether of a strengthening or of a sedative kind; the nervousness is not allayed by bromides; no ordinary prescriptions for dyspepsia relieve the gastric distress or flatulence; the diarrhœa is not checked by astringents; nor the insomnia helped by soporifics; while emaciation continues progressive, and the weakness grows apace, in spite of all restoratives. It is no wonder then, that the aid of surgery is invoked out of despair at the supposed inefficacy of medical treatment.

But what such conditions do prove is that one specific, underlying cause is the common origin of the whole array of symptoms, and so long as that specific cause is not dealt with, the separate treatment of the resultant symptoms necessarily can be of no avail. A close parallel obtains in the case of diabetes mellitus, for until the primary derangement in the metabolism of sugar is attended to, none of the many nervous or nutritive disorders of that disease can be even alleviated. Our chief aim, therefore, should be to determine what the one underlying cause of this disease is, and to make that the objective of our endeavors.

It was an unmistakable demonstration of the effects of diet in a serious, and ultimately fatal, case of Graves' Disease, which first led me to suspect that the toxæmia of Graves' Disease has its origin in the gastro-intestinal tract. This patient, whose history is given as Case I of the fatal cases with goitre (p. 102), after every remedy, medicinal or otherwise, ordinarily prescribed for Graves' Disease had been tried without success, began to improve at once, until she apparently recovered, upon her being restricted to the use of the Arabic fermented milk instead of meat. She

then resumed a meat diet and forthwith relapsed. Discontinuing the meat, and resuming the milk she rapidly improved again. She then refused to continue the use of milk, and returned to meat, with the result that her malady became uncontrollable, and soon ended in death. The relation of cause and effect in the quality of her food, as regards both improvement and relapse, was as clearly and repeatedly shown as would be desired in any instance of disease.

The dependence of the entire train of symptoms of Graves' Disease, not upon any state of the thyroid, but on what is ingested into the alimentary canal, can be experimentally tested at any time. Let a patient, with a temporary improvement in the symptoms of Graves' Disease, partake heartily of beef three times a day, and particularly at the evening meal; and directly it will be found that every one of the characteristic disorders will be as surely aggravated, as those of a diabetic would rapidly grow worse upon a free indulgence in starches.

Since abandoning almost entirely the employment of any mere symptomatic remedies, and adopting a system of treatment based upon the theory that Graves' Disease is due altogether to a gastro-intestinal disorder, my experience has come as near demonstrating to me the correctness of this view as would be possible from any facts in therapeutics that I know of. This verdict, to be conclusive, however, should be based only on results achieved in unmistakably serious, as well as chronic cases. Graves' Disease affects different patients in very varying degrees. A number of them improve under quite different measures of treatment, or with no treatment. Others improve for periods more or less prolonged, and then relapse. The cases which I would prefer as a test are those who are very ill, and so weak that they can scarcely leave their beds, whose tachycardia is extreme and persistent, or who have obstinate diarrhœa and great emaciation, accompanied with all the distressful nervous symptoms which belong to bad cases, and with whom everything of the nature of a symptomatic remedy has been tried before.

At the risk of seeming repetition, I give the following tables of results of my treatment of patients of both classes, the clinical details having already been given in the preceding pages in the

histories of those with, and those without goitre. I include here only those who have been my own patients throughout, and not those who were seen in consultation, with one exception among the cases with goitre, and one among those without goitre.

CASES WITH GOITRE.—25.

Females, 20; *Males,* 5.

1. M. W. 5 years' illness, goitre one year; recovery. Under observation eight years.
2. Mrs. G. Goitre one year; recovery. Under observation 15 years.
3. Mrs. W. Goitre 1½ years; recovery for 4 years; till death from pneumonia.
4. Mrs. D. Goitre persistent for 16 years; general improvement; goitre much diminished in size.
5. Mr. T. Goitre persistent, after 2 years; but great improvement in general symptoms.
6. Miss W. Great improvement during 5 years, with occasional relapses. Goitre disappeared with other symptoms, but patient became insane.
7. Miss P. Tachycardia for 10 years; goitre for 2 years; recovery.
8. Mr. P. Goitre 2 years; general improvement; ceased attendance after 2 years.
9. Miss C. Illness 2 years; goitre one year; recovery.
10. Miss H. Illness 2 months before goitre, lasting 5 months; recovery.
11. Mrs. B. Goitre 10 years; much improved; then relapsed; patient irregular about treatment.
12. Mrs. W. Goitre 2 years before treatment; severe general symptoms; persistent afterwards for 6 years; recovery.
13. Mr. S. Goitre one year, recovery.
14. Mr. M. Symptoms 4 years; goitre 2 years; recovery from all symptoms after one year's treatment.
15. Miss S. Goitre 8 months before treatment; entire recovery in one year; under observation for 5 years afterwards.
16. Mrs. P. Illness 4 years; goitre 2 years before treatment; severe case; marked improvement for 3 years; death subsequently from pneumonia.

17. Miss R. Goitre for 2 years; recovery, after 2 years' treatment.
18. Mrs. W. Severe case; goitre 3 years; recovery in the fourth year; under observation 5 years.
19. Miss B. Severe case; improvement and disappearance of the goitre in ten months. Several relapses in 3 years, with moderate return of goitre. General improvement, but tachycardia persisting after 5 years, with no goitre, but continued exopthalmos. This patient, however, was irregular in attendance, and in keeping up regimen.
20. Miss T. Graves' Disease for 6 months, supervening on chronic parenchymatous goitre. Improved in all respects after 2 years' treatment.
21. Mrs. B. Large goitre, with all other symptoms, but without tachycardia. Cured, with entire disappearance of goitre after a year's treatment. Under observation three years.
22. Mrs. W. Goitre for 3 years before coming. Refused all treatment, and became a confirmed paranoic.
23. Mrs. E. W. Severe case. Illness coming on for several years; goitre for one year before treatment. Recovery of weight and strength in little over a year's treatment; disappearance of goitre after a year and a half.
24. Mrs. D. Goitre for 4 years before treatment; great improvement in 14 months in all symptoms.
25. Mrs. P. Acute case of 2 months' standing; rapid recovery from dangerous state; goitre disappeared in eight months.

It is difficult to sum up these results, so as to tabulate them in a statistical form, because almost each case had its own peculiarities as regards the duration of the disease both before and after they came under my treatment. Improvement, however, was distinct in every one of them, the only exception being Case XXI, who refused to take any medication. The term recovery is given only to those in whom it was complete, with disappearance of the goitre, and this is noted in 17, or 70 per cent. Marked improvement, but some persistence of the goitre, in three; in only one of these was the goitre not diminished in size. Disappearance of the goitre, but persistence of moderate tachycardia in one.

Of the other fourteen in my original list, as they were not my patients, but were seen in consultation, I can give no particulars except that as far as I have been able to learn, improvement

occurred in all of them except four, two of whom would not continue treatment, and two died, but not from Graves' Disease.

CASES WITHOUT GOITRE.—18.

Females, 14; *Males*, 4.

1. Miss L. W. Severe case of 9 years' duration of symptoms, with final complete recovery.
2. Mrs. L. Two years' tachycardia, then prolonged diarrhœa with great emaciation. Improvement began soon after beginning treatment, with entire recovery after three years.
3. Mr. S. Tachycardia for five years, with the other symptoms; complete recovery after four years' treatment.
4. Mr. C. Symptoms of 8 years' standing; improved, but still with tremor of the right hand at the end of 9 years.
5. Mrs. H. Very severe case; symptoms preceding my first visit for two years and a half. Found patient in a very dangerous state of prostration, with extreme emaciation and tachycardia. Under constant and active treatment for seven months she began to improve, and in about 14 months seemed to have recovered entirely. She then remained in excellent health for four years and a half, when she had an acute and fatal relapse.
6. Miss B. Symptoms of four years' duration, with gradual improvement and final recovery.
7. Miss P. Treated by me for four years, from the beginning of her symptoms. No real relief, when she ceased attendance.
8. Miss M. Tachycardia and extreme nervousness, etc., with sudden beginning. Ceased attendance after two months' treatment, as she refused to continue the regimen.
9. Miss W. Chronic symptoms preceding treatment for a number of years. Afterwards entire recovery in three years.
10. Miss R. Symptoms for a year before treatment. Conditions typical of Graves' Disease. Continued treatment for nearly two years, with general improvement; but was not cured when she ceased attendance.
11. Miss K. Tachycardia for four years after beginning treatment. General improvement, with frequent relapses. Still calls occasionally for some of her old symptoms.
12. Miss M. Symptoms of two years' standing before treatment. Recovery after six months.

13. Mrs. S. Severe case of general and special symptoms; tachycardia first paroxysmal and then continuous. Entire recovery after two and a half years' treatment.
14. Mrs. C. Tachycardia and diarrhœa of four years' standing before treatment. Varied nervous derangements. Entire recovery after a year and a half of treatment.
15. Miss F. Intestinal derangement of long standing. Tachycardia for a year before treatment. Partial improvement in six months.
16. Mrs. M. No tachycardia, but all the other Graves' symptoms. Sister with Exophthalmic Goitre. Improvement in a year and a half. Death from acute pneumonia.
17. Mr. D. Severe general symptoms. Marked improvement in three months; relapse after discontinuing regimen.
18. Mr. W. Tachycardia for eight years, with chronic gastric derangement. Entire recovery in two years.

It will be noted in this table that the disease was more chronic, and the failures more in number proportionately than in the table of those with goitre. With the exception of Case VII, however, the failures to cure could be ascribed to the patients becoming weary of the prolonged course of regimen and of medication advised. As it stands, complete recovery occurred in 13, or 70 per cent.; improvement in 5, or 25 per cent.; no permanent improvement in 1, and one patient remained only six weeks under treatment. These statistics, however, fail to indicate sufficiently that among the complete recoveries were the most prolonged and severe cases. One of these, however, Case V, was restored for more than four years to excellent health after the most dangerous illness, but then died in a relapse. Case XI was also a severe case, but though greatly improved, ceased attendance before entire cure.

My original lists, of 70 of both classes, include two deaths among those who had goitre and two among those without goitre. But the first goitrous fatal case refused to continue treatment, with the result that she died after six months from a relapse. The second fatal case I saw in consultation only in the last week of her life, when she was too ill to take any remedies.

The first of the two fatal cases without goitre had been ill for a number of months, and lived only six days after I saw her. She was so far advanced in her disease that her constant vomiting

and diarrhœa made all administration of medicines, as well as nourishment, impossible, so that her death cannot be ascribed to failure of treatment.

It is not so, however, with the second case. For several years I regarded her as one of the most signal examples of the efficacy of proper treatment in rescuing a patient from the extremest dangers of Graves' Disease. After four and a half years of apparently excellent health, the same train of old symptoms returned. The only cause therefor, which I could learn, was that she became careless about her diet and was particularly averse to taking milk. Besides her old digestive troubles, signs of cardiac failure became more pronounced than in her former illness, and she died at last from syncope after two months continuance of her symptoms, which this time were but little affected by remedies. This case, therefore, shows that final recovery can not be regarded as certain in this complaint. Taken as a whole, therefore, my experience is that really developed cases of Graves' Disease, without Exophthalmic Goitre, are more difficult to treat than those with goitre. It is important on that account to make the diagnosis early, and, as we have remarked before, this can be done by the pathognomic symptom of persistent tachycardia, which then will be found so associated with the other symptoms, that the proper treatment can be adopted at once, with much better results than if the case be allowed to progress for an indefinite time with only symptomatic remedies.

It is always advisable to impress upon the patients from the beginning that their malady, when fully established, is not easy to cure, and that they will have to continue in the course recommended for at least two years, whatever improvement has been secured. Most patients of ordinary intelligence can be made to see that all derangements of digestion, if they have continued for a length of time, will then require time to correct them. Any diarrhœa, for example, whatever the original cause, which has lasted two years, cannot be expected to cease without prolonged attention to dietetic rules to prevent relapses, as well as to the prescribed remedies. Hence, in a disease characterized by so many different and chronic disorders as Graves' Disease, nothing

short of the utmost perseverance in a systematic course of treatment will insure ultimate recovery. I have always found that relapses occur only after the patients have violated the instructions about diet, as they would in any chronic disorder of digestion or in diabetes.

In accordance with the principles enumerated as regards the etiology and pathology of Graves' Disease, the systematic regulation of the diet ranks first in importance in the treatment of Graves' Disease. We should be as particular in drawing up a list of the admissible and of the non-admissible articles in the patient's dietary as we would with a diabetic, because without perseverance in this particular failure will follow as surely in the one disease as in the other. We would scarcely rely on drugs to neutralize the effects of a free indulgence in starches by a diabetic, and likewise the specific relation of Graves' Disease to the quality of food taken should be so strongly held that no other measures of treatment should be regarded as other than subordinate to that of diet. It is true that in mild and incipient cases, dietetic errors may for a while not seem to be of such consequence. But the same may be said of many diabetics. When the disease, however, has got a firm hold on the patient, if he continues to eat freely of red meats, such as beef, veal, mutton or pork, nothing becomes plainer than the futility of drugs, and especially those directed against mere symptoms. So long as the poison is formed in the digestive tract, and then absorbed into the blood, paralysis of all vaso-constrictors occurs throughout the body; the arterial system everywhere relaxes, and the whole train of vascular, nervous and secretory symptoms characteristic of Graves' Disease develop as a consequence.

The dietary of a patient with Graves' Disease by no means requires the vexatious restrictions of diabetes; and yet with all its latitude, it is often difficult to persuade the patients to adhere strictly to it. Like all other serious disorders of digestion, this one is apt to continue for prolonged periods, and with the first improvement in health, the patients are prone to relax the regimen and to ask for a change. They may do so on the advice of some medical man whose experience with the disease is limited, and who allows them to be guided by their appetites, or else by

friends who think that meat is strengthening for their weakness. I have repeatedly had patients, with a chronic history of the complaint, return to me in a wretched condition owing to their having followed such advice, more particularly those who have grown weary of a continued milk diet.

As milk constitutes much the safest food for this disease, enough to be by itself sufficient to cure many cases without any other treatment, its administration as a remedy merits more than a passing consideration. There can be no doubt that simple cow's milk cannot be taken as such by most adults in any considerable quantities for any length of time, without seriously deranging the digestion. This fact is well known, and acted upon by all races of men who have to live on milk as their chief article of food, such as the Bedouins, the Tartars, the Guachos of South America, etc., who subsist on the milk of cows, goats, sheep, mares and asses. Bedouins cannot be persuaded to drink fresh milk, any more than we would eat uncooked vegetables. They always ferment it first, and for a very good physiological reason. As fresh milk has first to be curdled in the stomach before it can be digested, any quantity of its uses up so much of the pepsin of the stomach that not enough then remains to dissolve the precipitated casein, and large masses of hard curds remain to disorder digestion, or as many express it, they are made "bilious" by it. By artificially curdling it first, the stomach is spared this step in the process of its digestion; and the ferment usually employed is yeast-plant. By some Tartar tribes the lichen, called keffir, is used instead, and an excellent article is made by it.

Throughout Western Asia and in Egypt, a piece of dough is commonly put in the milk to make the first specimen; but after that enough of the fermented milk is reserved each day to add to the milk as it comes from the cows to ferment the supply for the next day. When so prepared it is doubtful if there be any more digestible or complete food, for milk contains every ingredient in its due proportion out of which the body can be built up, as the growth of all young mammalia proves. With this fermented milk I have been able to cure some of the worst forms of gastric disorder, particularly those characterized by vomiting.

Even in cancer of the stomach, I have known it to be borne, when every other article of diet was rejected.[1]

Any one can learn to live largely upon fermented milk, as is demonstrated on an extensive scale by its universal use in Western Asia, Arabia, Egypt, etc., and I have found most of my patients become fond of it. Others, however, assert that they cannot bring themselves to continue its use; and many of them have used instead milk peptonized by Fairchild's peptonic powders. Others get along with milk diluted with an equal amount of Vichy water or lime water. Milk and cream can also be used freely with cereals, and is all the better digested if sweetened with sugar in moderate quantity. The aim in every case should

[1]Owing originally to my recommendation of this fermented milk, a number of Armenians have been supplying New York and other cities with it, under the names of leben, matzoon, zoolak, etc., while Dr. Brush, of Mt. Vernon, N. Y., manufactures extensively a preparation which he styles kumyss, as it more nearly resembles that used by the Tartars. As this preparation is bottled, it contains more carbonic acid gas than fresh matzoon and is apt to be more acid. But any one could make this milk for themselves after this fashion. Take half a cake of compressed yeast, and break it up in good fresh milk, warmed to 100°F. Put this aside in a pitcher covered with a wet cloth in the kitchen for twelve hours, by which time the milk will be fermented. It then tastes, however, too bitter from the yeast, and a second pint of fresh warmed milk has to be fermented by adding a proportion of one-third of the yeast-milk to it. When this is fermented, it is still too bitter to use; and a third of it has to be added to a third specimen, which when thus fermented generally is no longer bitter, but of a slightly acid and pleasant flavor. After this, all that is needed is to keep enough of the matzoon made each day to ferment the milk for the following day. The fermented milk should be well stirred into the fresh milk when it is added, and when it is fermented it can be put into a refrigerator to prevent its becoming too sour. Matzoon should preferably be *eaten* with a spoon as soup is taken, rather than drunk, and there is no objection to sweetening it with sugar, if preferred. I direct patients with Graves' Disease to take it as their first course with each meal, and not to use it too cold, as it is apt to be when first taken out of the refrigerator. After a time, particularly in warm weather, the yeast plant dies out and ceases to ferment the milk properly. When this is the case, usually not for some weeks after the first fermenting, a fresh yeast preparation has to be made, as directed.

be to ensure the use of milk as a chief article of diet, and particularly so at the evening meal.

Professor Chittenden has drawn attention to the fact that a smaller proportion of bacteria are found in the fæces, both in animals and in man, when fed upon milk than when fed upon any other diet, whether vegetable or animal. Clinical experience, from that of Charcot down, has borne constant testimony to the benefit of a milk diet in Graves' Disease; and I can only say that I always feel discouraged with a patient who continues to decline its use. Many assert that they never could take milk, but after explaining why ordinary milk is indigestible, and how it can be made to be one of the easiest of all foods for weak stomachs to deal with, they usually soon learn to overcome their objections.

Poultry, on the other hand, is usually well borne, provided that it be not kept too long. Fish, as a rule, is also allowable, excluding, however, the more oily kinds. Boiled fish is generally more difficult of digestion. Oysters usually agree well. No more than two eggs should be taken in a day. Bread is an excellent article, and can be taken freely with butter, but in all cases should be as crusty as possible. Of the cereals, oatmeal in any form should be avoided; but hominy, well boiled, and rice are good. The many so-called breakfast foods the patients must be left to themselves to judge of their effects. Of the vegetables, beans and peas are injurious, but string beans can be taken freely. Asparagus, tomatoes, beets, turnips, carrots and spinach are also to be avoided, though raw tomatoes in salad and baked tomatoes can be taken by many without disturbance. Stewed tomatoes are too acid. I have found potatoes generally well borne. When diarrhœa is persistent, the use of vegetables should be restricted until the looseness of the bowels subsides. I have not found diarrhœa so often induced by vegetables as by the taking of red meats; but when the bowels have become habitually irritable, all fruits and vegetables may require to be omitted for a time. In Graves' Disease, however, we meet with special idiosyncracies as to certain articles of diet, just as in other complaints; and hence the rule, that nothing which is tasted again in eructations from the stomach should be taken afterwards by that person, should be strictly observed, whether it be an article

of food or of drink. Cooked fruit is almost always well digested, but uncooked apples, pears and plums are very likely to cause diarrhœa. Strawberries and raspberries are to be taken with caution, but ripe blackberries and whortleberries usually agree very well, especially when taken with milk and cream. Coffee and tea, if taken well diluted with milk, are generally allowable; but many patients cannot take coffee at all. Pastry and cakes should be excluded, though I have found that light loaf gingerbread, taken with milk, agrees very well with many, perhaps on account of the ginger being a good intestinal antiseptic. The preparation called Mellin's Food, taken in hot milk, often relieves the morning headaches; and can be taken at other times between meals, when the patients feel weak or exhausted. All fermented alcoholic liquors should be avoided, and only spirits allowed in moderation, and never on an empty stomach.

The proper medicinal treatment of Graves' Disease affords one of the most conclusive proofs of the gastro-intestinal origin of this malady. As already remarked, I have witnessed nothing but failure follow the employment of such agents as digitalis, belladonna, ergot, aconite, and veratrum viride against the tachycardia. I may add that the administration of bromides and of chloral, I have found in time as injurious to the general health, as they are unavailing for permanent relief either of the nervousness or the insomnia; while for the progressive weakness and emaciation of severe cases, no benefit accrues from any of the so-called tonics or restoratives, such as iron, phosphorus, quinine, strychnine, cod liver oil, arsenic, or iodine. An exception might be allowed in the case of aconite, when the pulse is too strong, and strophanthus is sometimes beneficial against palpitation; but these are only symptom remedies and scarcely affect the disease itself.

In complete contrast to the inefficacy of all such merely symptomatic remedies stands the prompt and unmistakable effect of agents which can act only through modifying conditions in the gastro-intestinal tract. Thus the heart quiets down immediately after the action of a mercurial cathartic. The statement of Dr. J. P. Thompson, in his letter describing Case VII (p. 50) of Exophthalmic Goitre, that the pulse fell 40 beats after the first

blue pill taken, I have had paralleled repeatedly in my experience. So consistently has marked improvement, not only in the tachycardia, but in the other leading symptoms, followed upon mercurial laxatives, that my notes on this point are as follows:

Whole number of cases with goitre recorded, who took mercurial laxatives once a week throughout treatment, 18. Improvement in all, except one, who could not take it on account of the effect on her teeth.

Whole number of cases without goitre, 20; and they failed to give relief only in one case.

It is equally noteworthy that the beneficial action of mercurial laxatives is not restricted to their first employment, but continues upon their use for months and years, the patients continuing to report that they felt better after them throughout their entire illness. The presence of diarrhœa, instead of contraindicating the administration of mercurial laxatives, is most satisfactorily relieved by them; and far more certainly than by any astringents.

The only explanation why a mercurial laxative can so favorably affect a persistent over-action of the heart, relieve mental depression better than any stimulant, and calm nervousness and tremor, is that mercurial laxatives are among our best established intestinal antiseptics. I am yet to meet with a case of Graves' Disease in which their administration aggravated any condition in the patient. With most patients I prescribe the 5 gr. blue pill, taken at night, followed by a saline in the morning; or with others, a grain and a half of calomel, rubbed up with cane sugar, and divided into six powders, one to be taken every fifteen minutes till they are finished, and then a saline to be taken three hours after the last dose. It is very common for patients to say that they feel the benefit of the mercurial more on the second than on the first day after taking the dose. That it is not the mere taking of a cathartic, which causes the good effects, is shown by the fact that no other than a mercurial laxative, with the exception of castor oil, is followed by any such pronounced improvement in the constitutional symptoms. To many patients I prescribe the mercurial twice a week, while to all others at least once a week. With some patients, castor oil seems to act better than a mercurial cathartic. This can be found out only on

trial, or it may in others be given alternately with the blue pill. Occasionally half a grain of podolphyllin well triturated with ten grains of sod. bicarb. is good for a change. In some cases of insomnia, a grain of calomel with two teaspoonfuls of pulv. glycerrhiz co. taken at bed-time acts as an excellent soporific. Marked general weakness does not contro-indicate the use of these cathartics, owing to their counter-acting the primary cause of the systemic prostration.

Gastric flatulence and discomfort are symptoms which often continue to be very obstinate and persistent. The whole list of vegetable bitters may be discarded, including nux vomica or strychnia, nor are the mineral acids of much use. I have also been as frequently disappointed with pepsin, nor am I certain that its administration in my experience has ever been plainly efficacious. I may say the same of charcoal, which I have repeatedly tried and found of no avail against the gaseous distension of the atomic stomach walls. Gastric lavage I never prescribe, for many of the patients who have come to me have had this procedure faithfully tried before, with the invariable story that no mucus was brought away in the washing, and that they felt weakened and much worse after the operation. As it is a constant characteristic of Graves' Disease that its various visceral derangements have no inflammatory element connected with them, the failure of the different measures, often useful in other forms of gastric disorder, is not surprising.

The medicines which I have found most efficacious are the bismuth subcarbonate in ten to fifteen grain doses, taken just before eating, with a pill of one twentieth of a grain of bichromate of potash, with two grains of cerium oxalate. Occasionally, a drop of Fowler's Solution may be given also. Not uncommonly, sodium phosphate, 20 grains, before eating, acts well. Resorcin, on the whole, however, has oftenest stood in good stead against troublesome flatulence, and there is no objection to add the tincture of nux vomica, as in ℞ Resorcini 3ii, Tr. nucis vomicæ, 3ii, Syr. zingiberis 3xii; Aq. menthæ; ad. ℥vi S.

Two teaspoonfuls in wine glass of water half an hour after meals. Some patients have found this useful also in the night if awakened by stomach distress. I must say, however, that resor-

cin is not nearly so efficacious in the stomach troubles of Graves' Disease, as it is in gastritis, in which I consider it to be the best of all medicines, and yet from its antifermentative properties it is not without use in Graves' Disease also.

Among our intestinal antiseptics bismuth must always take the first rank. But I have found its combination with phenol deritives especially useful. Such preparations as ten grains of phenol bismuth, or naphthol bismuth, with the same doses of sodium or of ammonium benzoate, in two capsules, taken an hour after meals and on retiring to bed, or forty grains of each per diem, have been taken by a number of patients with benefit for months at a time.

There can be no question also of the great value of the salicylicates in Graves' Disease. In acute Graves' Disease, when the onset of the symptoms is both rapid and severe, the sodium salt should be prescribed as freely as in a case of acute rheumatism, the dose being lessened, or the preparation changed as the disease becomes subacute. I think that in one such case, seen in consultation, when the history of the goitre was only of six weeks' standing, with extreme pain in the thyroid, with a daily afternoon rise of temperature to 103°F., and great prostration, that I saved the life of the patient by prescribing the administration of this drug every two hours. On the other hand, the muscular pains and stiffness which are so pronounced in many of these patients, I have found better relieved by the strontium salicylicate in fifteen grain doses, than by the sodium salt; and it has the advantage of being less depressing.

Second only to the salicylicates, I would rank the benzoates. As both the sodium salicylicate and the sodium benzoate are efficient cholagogues, I have been accustomed to give ten grains of each in capsules an hour after meals, in the treatment of migraine as a prophylactic of the attacks. I also prescribe in the systemic and curative course for the disease migraine, in contrast to symptomatic prescriptions for the attacks themselves, a weekly dose of blue pill or of castor oil and a morning dose on rising of ℞. Sod. phosphas. ℥i, Sod. sulphas 3iv, Sod. salicylicas 3ii. Div. in chart. XII. S. One powder in a tumbler of *hot* water, sipped slowly. These same prescriptions of the morning salts and of

the capsules are very commonly given by me to those Graves' patients who suffer much from headaches, for, as already mentioned, I regard these headaches as distinctly migrainous in character, while migraine itself is allied in its etiology to the underlying cause of Graves' Disease.

The sodium phosphate in quite a proportion of patients seems to assist their digestion, in 3ss. doses taken just before meals, particularly in the class without goitre.

Other intestinal antiseptics will occur to experienced prescribers, such as sod. sulphocarbolas, ichthyol, etc., and in many cases it is best, when the symptoms are predominantly intestinal, to have the drugs put up in shellac-covered capsules.

The only iodine-containing prescription which I prescribe is aristol in from one to two grain doses. Some of my patients have stated that the sodium and gold chloride in 1-20 grain doses, t. i. d., put up in capsules with 3 grains of sugar of milk, relieves their nervousness better than anything else.

I would append a synopsis of the treatment of a patient, who might fairly be classed as a serious case, as an illustration of the management of the varying conditions throughout. When first seen by me September 26, 1901, she had had a large goitre, more in the right lobe, for over a year, but no exophthalmos. She had become so emaciated that she only weighed 81 pounds; and as she had suffered from bronchitis, with constant cough for five months, she greatly resembled a case of advanced phthisis. The pulse was 110, very forcible and rather incompressible. She was extremely nervous and insomnic, and so weak that she had frequent falls. One of her chief complaints was the tinnitus, particularly in her left ear, etc.

She began September 26 with the fermented milk as a chief article of diet. As she was constipated, Sod. phosph. ℥ii; Sod. salicylicas 3ii; t. chart. xii. S. One in hot water every morning. Blue pill once a week at night, and ℞. Ammon. benzoas 3iv, Ac. salicylic 3i, Phenol. bismuth 3iii, M. Div. in capsul. xlviii. S. Two an hour after meals.

September 30.—After blue pill pulse fell to 82; now 96. Feels less nervous, but sleep bad. To take for this: ℞ Strontium

bromide 3iii, Resorcin 3i, A. menthæ ad ℥vi. S. Tablespoonful in water. t. i. d.

October 12.—Better, growing in weight. Continue treatment.

October 20.—Better in all respects, but complains greatly of both tinnitus and pain in left ear. To apply blister to left mastoid. Pulse 94.

October 23.—Pulse 110. Complains of nocturnal palpitation, tinnitus and insomnia. To change to ℞. Sod. suphocarbolas 3ii, Kal. permanganas grs. xxiv, in 24 shellac-covered capsules. One, half an hour after meals; and ℞. Phenol bismuth 3iv, Sod. benzoas, strontii salicylicas āā 3ii. Div. in capsul. xlviii. S. Two one hour after meals. But last dose at night.

October 28.—Has gained 7 pounds since October 12. But still insomnic. To take at night for three nights, 3ss. strontium bromide and gtts x tr. strophanthus for palpitation.

November 7.—Improving in every way; stronger, so that she can sit out of bed for several hours. For palpitation to try strophanthus 4 times a day.

November 11.—Has gained 6½ pounds more in two weeks; feels much improved; tinnitus better; pulse 100, but increases after eating. Goitre diminishing in size.

November 16.—Not so well, from increased palpitation. To omit the strophanthus, and take tr. aconite gtts v night and morning.

November 21.—Marked improvement. Pulse down to 82 and softer.

November 25.—Continued improvement. Better sleep, which she ascribed to the aconite.

November 30.—Continued improvement; says that every time she takes the blue pill she has less palpitation.

December 7.—Some strain after illness of her husband, with increased indigestion; pulse 88; to take for flatulence extra dose of resorcin.

December 12.—Doing well; increase of 4 pounds in two weeks; Pulse 92, to take aconite. t. i. d.

December 16.—Improved in every respect, except the tinnitus; especially at night.

December 31.—Better in general; weight increased now to 114

pounds; but tinnitus very troublesome, in spite of temporary improvement from strontium bromide, ergot and gelseminum tried alternately.

January 9, 1902.—Quite depressed with a relapse; pulse 106 and forcible.

January 14.—Sharp attack of bronchitis, with bloody expectoration. T. 99°. Pulse 106. This cough and bloody expectoration continued till Jan. 20th. She meantime omitted all capsules. On Jan. 20th the bronchitis was promptly relieved after taking: ℞ Ac. nitria dil. 3ii ss. Kal. iodidi grs. xlviii, Syr. zingiberis 3i ss., Aq. menthæ ad ℥vi. S. Tablespoon in water. t.i.d. Meantime she was to resume all her medicines for Graves'.

January 29.—Another relapse of bronchitis. To resume the ac. nit. mist with the addition of gtts. 10 tr. belladonna to each dose.

February 1.—Pulse down to 78; omit nitric acid.

February 13.—Continues to improve.

March 8.—Went South till the 21st. Improved, but cannot leave off the capsules of am. benz. and phenol. bismuth with the sulphocarbolate 10 grs. at night.

April 1.—Disappointing story; excessive gastric flatus, insomnia, palpitation and morning mental depression. Pulse 102; borborygmi very annoying.

April 7.—Great flatulence still; to try castor oil instead of blue pill.

April 15.—Felt much better from the castor oil. Pulse now 82.

April 25.—Comes improved in every way; to continue the castor oil and the rest.

May 5.—Gaining strength, weight and color, but still complaining of the tinnitus.

May 29.—Has been doing very well, tinnitus at last diminishing; pulse 88. To take before meals 10 grains of powdered columbo, and 10 of bismuth subcarbonate, with one grain of aristol in two capsules.

November 22.—Comes to office almost transformed; increase in weight from 81 pounds to 142½ pounds. Tinnitus, however, continues; pulse 82; goitre one-third its former size. To continue the capsules before meals, and the old ones (Sept. 26) after.

January 10, 1903.—This patient considers herself well; goitre gone; weight 150 pounds; pulse 78.

I have no doubt that considering her continuous decline, in spite of previous symptomatic treatment by several well known physicans, that a surgical operation would have been considered by many as the only resource left. But when I first saw her, I doubt if any surgeon would have cared to risk such an operation, with her extensive bronchitis, her extreme emaciation, and her weakness so great that she was unable to walk more than a few steps at a time.

SURGICAL TREATMENT.

The different surgical procedures which have been undertaken for the cure of Exophthalmic Goitre, of course, are based upon the theory that the seat of the disease itself is in the thyroid gland. But a not uncommon attendant upon these operations is a remarkable and very fatal complication, to which the name of acute thyroidism has been given. The symptoms of this state are: that though the patient may have been put to bed in good condition after the operation, the temperature soon begins to rise to 102°, 103°, and in twenty-four hours to 104°, and then continues to rise to 106°, 107°, until it may reach after death, 110°. Meantime great restlessness develops, with the pulse running from 130 to 200, the breathing becomes very hurried and superficial, and the face flushed. The consciousness generally remains clear to the end, death being sudden from heart failure, or from rapid pulmonary edema.

This so-called acute thyroidism has been supposed to be a further confirmation of the theory of excessive thyroid secretion, by ascribing the fatal symptoms to a sudden poisoning from direct inoculation of thyroid juice into the torn vessels, or from too free absorption caused by the necessary handling of the gland during the operation. In a former publication on Graves' Disease (N. Y. Med. Journal, Oct. 10 and 17, 1896), I state that this statement has to rest on quite a number and variety of theories, namely: 1. That the thyroid secretes a hyperpyrexial poison at such times, which it never did before, as the tachycardia and other derangements of Graves' Disease are characteristically non-febrile. 2. This poison is not secreted, or at least absorbed, from the cut surfaces in the operation, except in those who die from this condition, because those who recover after being equally cut do so without any hyperexia. 3. Therefore, the thyroid secretion in Graves' Disease, when taken up directly from the

cells of the gland by open veins, acts very differently from the same secretion when absorbed in the usual way.

Against this theory of thyroid juice poisoning stands the fact that a fatal hyperexia occurs frequently as an accompaniment of derangement of bulbar centers, without connection with toxæmia of any kind. Some ten cases have been reported of convulsions ending in death, with temperatures ranging from 107° F. to 111° F. after washing out of the stomach, and 45 such cases after washing out of the pleura. The only explanation of these accidents is that a reflex excitation of bulbar centers is some times thus set up by totally unusual afferent impressions from the stomach and pleura respectively. As the experiments, above cited, of Filhene and others show that the thyroid is very intimately associated in its innervation with the restiform bodies, it is quite conceivable that the medulla may become more than usually susceptible, in a long standing case of Graves' Disease, to the shock of such a grave operation as thyroidectomy. But as far as the theory of thyroid juice poisoning is concerned, it has recently received its quietus by the occurrence of just the same fatal "acute thyroidism" in patients upon whom the operation of sympathectomy has been performed, without the thyroid being involved in the operation at all; and where, therefore, there could have been no addition of thyroid juice to the blood. Prof. B. Farquhar Curtis, of New York,[1] reports eleven thyroidectomies performed by him for Graves' Disease, with three deaths, or 27.2 per cent., all from "acute thyroidism." "Alarmed at the frequency of acute thyroidism," he writes, "and attracted by the immediate good results claimed for sympathectomy," he has performed the latter operation in seven cases; but of these seven, two died from "acute thyroidism" and one probably from the anæsthetic. As both cutting into and handling of the thyroid in these seven operations were carefully avoided, it is evidently a misnomer to apply the term "acute thyroidism" to the unfortunate outcome of a surgical procedure with which the thyroid had nothing to do.

The theory on which sympathectomy is based is an old one,

[1]Transactions of the Am. Surgical Association, 1903.

which we have already discussed (p. 117). By the operation of excision of the cervical sympathetic ganglia on both sides of the neck, it is proposed thereby to lessen the hyperæmia and hyperplasia of the gland, and thus check its supposed hypersecretion. The statistics of this operation are yet too few to be of much service. The most favorable reports are Jonnesco's, of 13 operations by himself, to which may be added four others by French surgeons.[1] One died, it is stated, from chloroform. Of the others, 10 are reported as cured, 5 improved, and 2 not improved. Curtis, as reported, performed this operation on seven patients, three of whom died, one, it is supposed, from ether, and the other two from "acute thyroidism." Of the remaining four, the first at the operation had a pulse of 76-88. A year after the operation, the tremor and nervousness were much improved; goitre somewhat smaller; increasing murmurs about the heart. The second, had a history of operation on December 2, and discharged December 22, with improvement in both eyes and goitre. The third, when seen five months after the operation, had the eyes less prominent; but still had goitre; with pulse 120. While the fourth, when seen five months after the operation, had the goitre but slightly diminished; exophthalmos, especially in one eye, much less; pulse 100.

I do not see how this record, with mortality of 43 per cent., without a single cure in the rest, can be regarded as other than a serious condemnation of this operation.

In thyroidectomy, the rule is to remove one-half of the hypertrophied gland, and, in some cases, with partial section of the other half. Ligature of the arteries, either before or at the operation, is also frequently performed, so as to lessen the overgrowth of the gland. Thus, in Kocher's 59 operations for Exophthalmic Goitre, he performed thyroidectomy of one-half in 14 cases; litigation of arteries in 16 cases; both at once in 19 cases. Thyroidectomy of one-half, with part resection of the other, in 4 cases. The same with ligature in 3 cases; ligature and partial resection in 1 case; ligature and partial sympathectomy in 3 cases.

As regards thyroidectomy, general statistics must be pro-

[1] Curtis, loc. cit.

nounced as very unsatisfactory, particularly as regards the proportion of deaths, as we cannot be sure how many unsuccessful cases fail to be reported. I know of deaths from thyroidectomy for Graves' Disease in this city alone, none of which have been published. In M. A. Starr's list published in 1896,[1] of 190 cases, the deaths from "thyroidism" were 23, or 12 per cent. Of these 190 cases, 74 were pronounced as completely cured, some having been watched subsequently from two to four years; 45 are described as improved, and 3 not benefited.

Rehn[2] gives the mortality of 95 severe cases of the picked operators series (not including Kocher's) as 21, or 22 per cent. Of 114 cases collected from literature, the mortality was 11.4 per cent. The cures were 54.8 per cent., and 27.9 per cent. were improved.

The most marked success by a single operator is that of Kocher, who operated upon 59 patients, with a death rate of 4 cases, or 6.7 per cent. He gives 76 per cent. as cured, 14 per cent. improved, and 3.3 per cent. slightly improved.

It would be tedious, as well as unprofitable, to analyze these reports, particularly Kocher's, for his remark that a "Basedow's disease, without swelling of the goitre, is unknown to us," shows that he studies this disease solely with a surgeon's eye, and therefore, in a country where parenchymatous goitre is endemic, a mere surgeon's diagnosis should be taken with qualifications. I have myself repeatedly been in doubt for some time, whether a case of goitre was parenchymatous or one of Graves' Disease, for parenchymatous goitre patients often have a temporary tachycardia, or are nervous when first examined. Thus Case IV of Curtis' series of thyroidectomies, I would not regard as a case of Graves' Disease at all. The swelling began of the size of a cherry only four months before. At the time of the operation, the eyes were natural, pulse only 80, general health good, bowels regular, and no tremors or nervousness are mentioned. The gland after removal was found to be finely cystic.

But the true test of the value of surgical procedures is to be found in the positive results obtained in certain unmistakable

[1]Med. News, April, 1896.
[2]Quoted by Curtis in loc. cit.

cases of Graves' Disease, for such positive results outweigh even the high percentage of deaths when the question is whether a thyroidectomy can be useful at all. And that such positive results have followed this operation there can be no question. Whether, therefore, the constitutional symptoms of Graves' Disease be due to excess of thyroid secretion, or to an entirely different cause, namely: to atrophy of the parathyroids, with deficiency of their secretion, or to a toxæmia of gastro-intestinal origin, the empirical fact remains that resection of one-half, or more, of the hypertrophied gland substance has been followed, in numerous instances, on the testimony of competent observers, by amelioration of the constitutional symptoms amounting, it is claimed, to a supposed cure of the disease itself in the majority of those operated upon, and in other cases to undoubted improvement, with a comparatively small percentage of failures.

My own explanation of these favorable results is that they have the same significance, as far as the etiology of Graves' Disease is concerned, that excision of an enlarged spleen has upon the etiology of hypertrophy of that ductless gland. There are a number of different causes which lead to chronic enlargement of the spleen, just as there are different causes of goitre. But whatever the original cause, a persistently hypertrophied spleen becomes itself injurious to the system at large, quite apart from its local effects upon contiguous organs, so that total excision of the organ often seems to remove a standing source of blood poisoning. That the thyroid and its accessory glands, whose functions are so closely related both to metabolism and to the neutralization of toxins, on the one hand, and to important nerve centers, on the other, should be even more injurious when largely hypertrophied than an enlarged spleen, is conceivable enough.

Ablation of the diseased tissue might then be as beneficial in its case, as it often is in the corresponding ductless gland. But, further than this, I cannot allow, on account of the numerous sources of fallacy in all statistics on results in Graves' Disease. In the surgical statistics, including Kocher's, I find whole series of cases reported as "cured," with more than one of the characteristic disorders of the malady still present, and which I would

not admit in my list as more than improved. Still more suspicious is the short time allowed for the cure. Whoever has had any prolonged experience with this disease knows only too well its proneness to relapse after apparent entire recovery for, it may be, years. With many patients if the disease though pronounced, yet has not involved the vital functions too seriously, spontaneous improvement is not uncommon. The only satisfactory tests, therefore, as I have remarked before, of the merits of any remedial procedures, whether medical or surgical, should be found in the really serious cases, where the general health and nutrition are gravely affected, so that a spontaneous recovery is very unlikely. But it is in just such cases that surgical operations are so dangerous. Were the surgical statistics limited to operations on such patients, the death rate would be simply prohibitory; and it is in the like of them, as I confidently maintain, that the medical treatment outlined above will prove to be the most efficacious. In such patients, medical treatment, if directed only against the symptoms, will fail. The true course is to let the symptoms alone, with only occasional prescriptions for their relief, while every endeavor should be perseveringly followed up which aims at counteracting the one underlying cause of the symptoms in a general toxæmia of gastro-intestinal—and not of thyroid—origin.

When the general systemic conditions, which exist in an advanced case of Graves' Disease, are considered, I do not know of any class of patients who would be less promising subjects for a severe surgical operation; or, who under proper medical treatment would not in time show how needless it is to run such risks.